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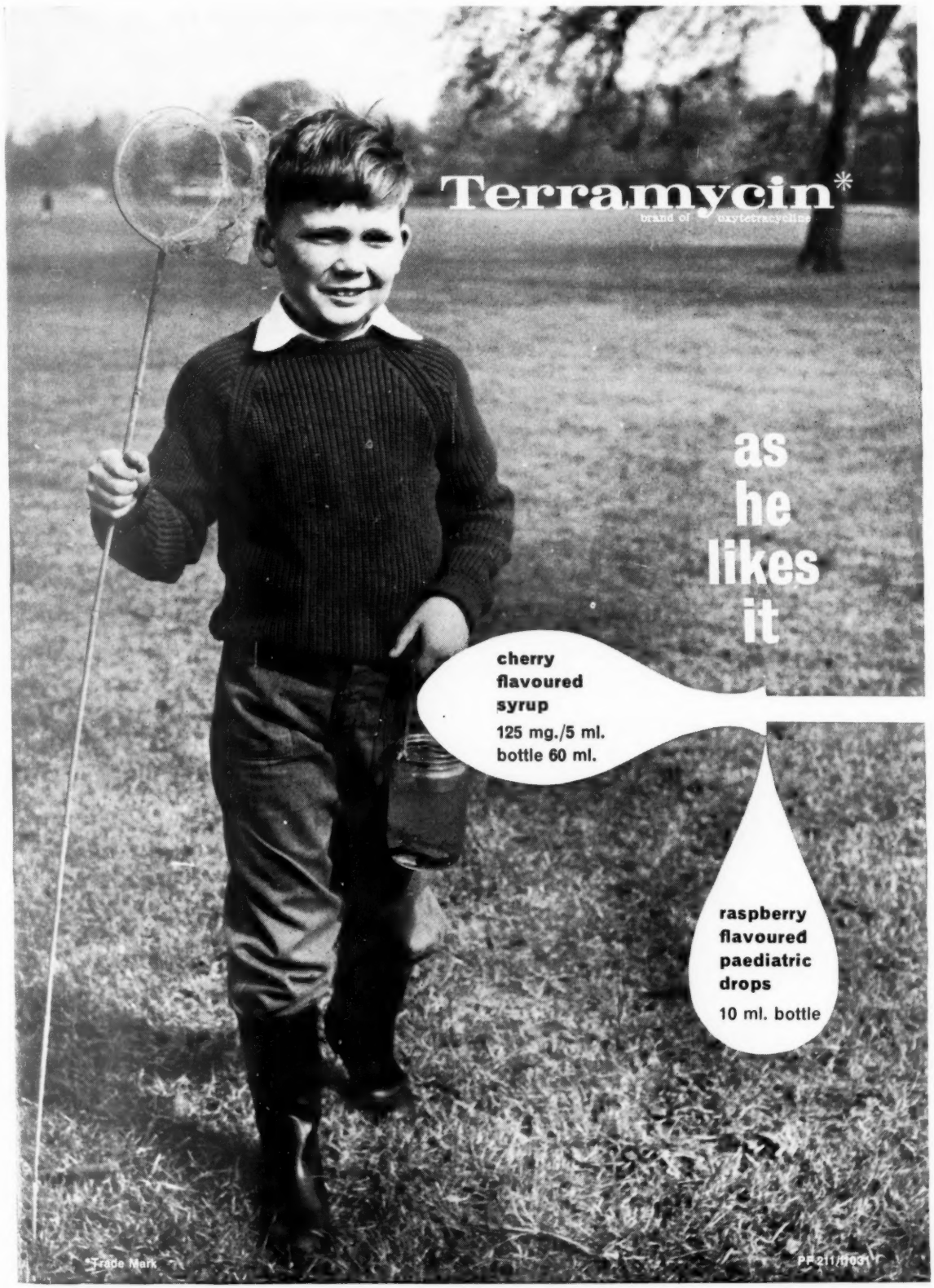

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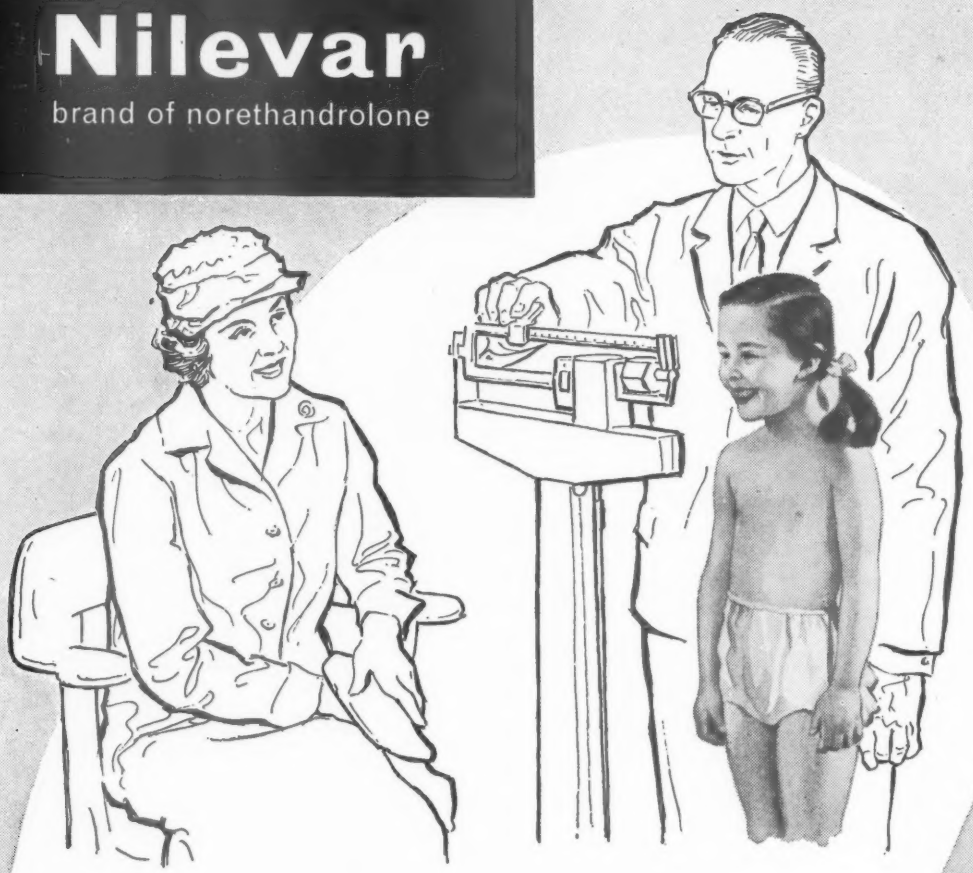

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ACUTE HAEMATOGENOUS OSTEOMYELITIS WITH SPECIAL REFERENCE TO OSTEITIS OF THE NECK OF THE FEMUR*

BY

J. H. LOUW and B. SHANDLING

From the Department of Surgery, University of Cape Town

Acute haematogenous osteomyelitis is still a common disease in Cape Town. During the past eight years we have treated 331 cases (351 bones) in the University of Cape Town teaching hospitals; 85% of these were children of 12 years and under, the disease accounting for 3·3% of the admissions to our Children's hospital where we have set aside a special ward for patients suffering from osteomyelitis.

Not only is the disease common but it seems to be increasing in frequency and in severity. Thus there has been a steady increase in the annual admissions (Fig. 1) and, whereas in 1949 only 24% of our cases were regarded as severe (Du Plessis, 1953), in 1959 the proportion had increased to 57% (Shandling, 1960).

Our cases have recently been reviewed by one of us (Shandling, 1960), and our findings in regard to age and sex incidence, social status, pre-existing septic foci and predisposing trauma are in keeping with those of others (Altemeier and Helmsworth, 1945; Agerholm and Trueta, 1946; Caldwell and Wickstrom, 1950; White and Dennison, 1952; Dennison, 1952; Trueta and Morgan, 1954). The bones most commonly affected were upper tibiae, lower femora and tibiae and upper femoral shafts (Fig. 2). In this paper we wish to discuss osteomyelitis of the neck of the femur of which we have had 27 cases (28 bones) since 1952. Before doing so, a consideration of the racial incidence of osteomyelitis may be of interest.

Racial Incidence

The population of Cape Town (Fig. 3) consists of 41% (310,000) Whites of European origin, 43% (340,000) Coloureds (mixture of original South African Yellow races, Whites and Asiatics) and 14% (107,000) Bantu (Negroids). As far as osteitis is concerned, we found 16% (53) in Whites, 80% (267) in Coloureds and 4% (11) in Bantu. This might suggest a racial predisposition as far as the Coloureds are concerned, but it is in fact a social and economic problem. It has long been noted that osteomyelitis is a disease of the poor (Mitchell, 1928), and Stevenson (1946) has pointed out that the disease is rare in private practice. In Cape Town, osteomyelitis is rare in the wealthier private patients and practically all our Coloured hospital patients come from very poor homes where lack of cleanliness and undernutrition are rife. On the other hand the Bantu children live in similar, often worse, circumstances and yet the disease is rare among them.

Osteomyelitis of the Neck of the Femur

Our 27 cases of osteomyelitis of the neck of the femur have followed the usual pattern. All the

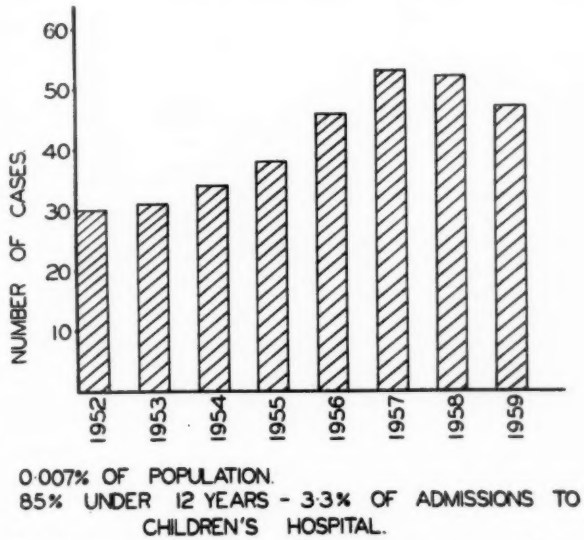


FIG. 1.—Annual figures of acute haematogenous osteomyelitis from University of Cape Town series 1952-1959—331 patients.

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

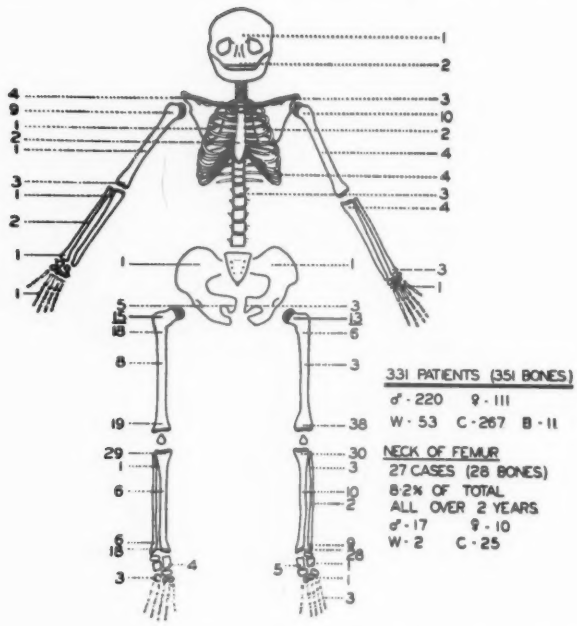
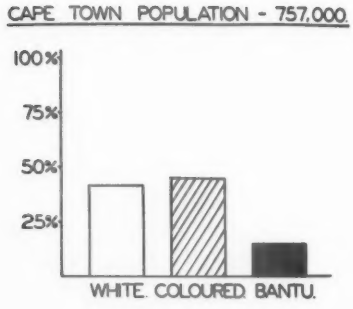


FIG. 2.—Diagram of bones involved in a series of 331 cases of acute osteomyelitis.



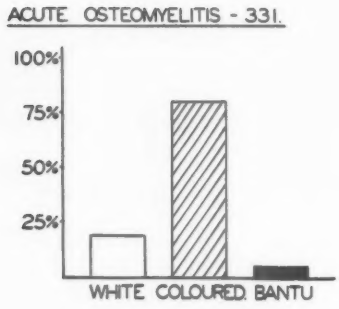


FIG. 3.—Racial incidence.

patients were over 2 years of age (comprising 9% of our cases of osteomyelitis in patients over 2 years) their ages ranging from 3 to 14 years with the highest incidence in the 10- to 12-year-olds (12 cases). Twenty-five were Coloured and two were White (no Bantu); there were 17 males and 10 females. It has often been pointed out that osteomyelitis in infants under 2 years differs from the disease in older children (Ober, 1938; Trueta and Morgan, 1954) and we wish to make it clear that the following remarks apply only to the older age group.

Bacteriology. The infecting organism was cultured from the patients' blood and/or pus in 24 cases and was found to be the *Micrococcus pyogenes aureus* in all (Table 1). In 16 (66%) it was sensitive to all the antibiotics including penicillin, in seven it was sensitive to streptomycin, chloramphenicol, tetracycline, erythromycin and novobiocin, but not to penicillin, and in one to chloramphenicol and erythromycin only. (In our cases in general the *Mic. pyogenes aureus* was the responsible organism in 98%; it was sensitive to all the antibiotics including penicillin in 82%, to streptomycin, chloramphenicol, erythromycin, tetracycline and novobiocin, but not penicillin in 14% and to chloramphenicol and erythromycin only in 4%.)

Clinical Presentation. The clinico-pathological features are conveniently divided into three groups (Table 2) depending upon the general condition of the patient on admission to hospital: (1) Bacteraemia and inflammatory fever; (2) septicaemia, or (3) severe toxaemia.

(1) BACTERAEMIA AND INFLAMMATORY FEVER—11 CASES. The general condition of these cases varied considerably. Some were quite ill with temperatures of 102 to 103° F., but not as severely ill as those in the septicaemic group. In others the general signs of inflammation were only slight with temperatures of 100 to 101° F. Leucocyte counts varied from 7,000 to 25,000 and the sedimentation rate from 35 to 100 mm. in the first hour (Westergren). The average duration of illness was four to five days (two to 10 days). Blood cultures were positive in two cases.

The local symptoms and signs depended upon the stage of the local lesion and although always definite, were sometimes difficult to detect because the neck of the femur is so deep seated and well padded by muscles. Not infrequently the diagnosis had at first been missed because of a lack of awareness of its possibility and failure to search for the tell-tale physical signs.

TABLE 1
BACTERIOLOGY

Organism	Sensitivity*	All Cases (%)	Neck of Femur (24 Cases)
Micro-pyogenes aureus	All antibiotics	81	16 (66%)
	S.C.T.E.N. (*not* P.)	12	7 (29%)
	C. and E. only	4	1 (5%)
Beta-haemolytic Streptococcus	All antibiotics	1·5	—
Streptococcus viridans	All antibiotics	0·5	—
Klebsiella aerogenes	S.C.T.E.N. (*not* P.)	0·5	—
Proteus Sp.	S. and C. only	0·5	—

*S = Streptomycin
C = Chloramphenicol
T = Tetracycline
E = Erythromycin
N = Novobiocin
P = Penicillin

TABLE 2
CLINICAL PRESENTATION

Presentation	Cases	Duration of Illness (days)	Positive Blood Culture
Bacteraemia and inflammatory fever	11	4–5 (2–10)	2
Septicaemia	12	2·5 (1–4)	10
Severe toxaemia	4 (5 bones)	9 (6–18)	1
Totals	27 (28 bones)	6 (1–18)	13

TABLE 3
FORMATION OF PUS (27 BONES)

Presentation	No. Drilled	Pus Found	Positive Culture
Bacteraemia (11 bones)	11	9–6 intra-osseous only 3 intra- and extra-osseous	7
Septicaemia (11 bones)	11	11–5 intra-osseous only 6 intra- and extra-osseous	8
Toxaemia (5 bones)	5	5– all intra- and extra-osseous	3
	27	25–11 intra-osseous only 14 intra- and extra-osseous	18

Pain in the region of the affected hip and a limp or inability to use the limb were constant and present at all stages of the disease. During the early *stage of acute inflammation, before the formation of pus*, the only objective signs were pain on passive movement especially internal rotation and extension, and tenderness over the neck of the femur. The latter sign is detected by deep palpation between the ischial tuberosity and greater trochanter of the femur (Fig. 4). Two of the patients in this group were first seen at this stage and the duration of their illness was two days and four days. On the other hand there were three cases with histories of only two to three days where the disease was already at a more advanced stage. It is thus obvious that although the duration is an important factor, time alone cannot be the only guide to the stage of the disease.

Our experience has led us to believe that any signs in addition to local pain and tenderness indicate the presence of pus. When there is *intra-osseous pus formation*, oedema is usually the first clinical indication: if the bone is superficial this is manifest as pitting oedema, but if the bone is deeply situated there is only vague swelling. In osteitis of the femoral neck this important physical sign is often not obvious until a somewhat later stage, but will be detected earlier by measurement and assessment of the thickness of the skin (Fig. 5). Although intra-osseous pus was present in the remaining nine cases in this group (Table 3), swelling could not be detected in two of them. In these two cases the presence of pus was diagnosed

FIG. 4.—An early and constant sign in osteomyelitis of the femoral neck is tenderness on deep palpation between the ischial tuberosity and greater trochanter.

FIG. 5.—Slight swelling is detected by measurement and assessment of the thickness of the skin.

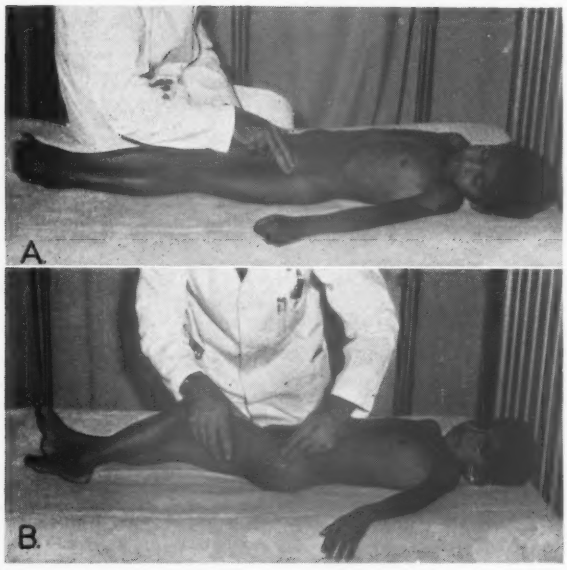


FIG. 6.—In more advanced cases the tenderness and swelling are present over Scarpa's triangle (6a), and the upper femur (6b).

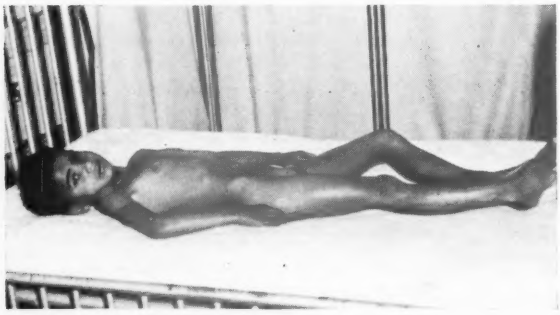


FIG. 7.—The hip is held in slight flexion, abduction and external rotation.

by assessing the response to conservative treatment as recommended by Trueta and Morgan (1954). The extent and intensity of the bone tenderness were accurately determined and recorded. The patients were then put on intensive antibiotic therapy. After 12 hours and 24 hours the same surgeon re-examined the patient. An increase in tenderness after 12 hours in one case and no marked decrease after 24 hours in the other, led to the correct diagnosis of intra-osseous pus formation.

Other signs of pus formation are local heat, redness and dilated veins. These are also more commonly seen in superficial bones and prompted Rutherford Morison's (Morison and Saint, 1935) aphorism: 'Cellulitis in a young limb means osteitis'. In the case of the femoral neck, however, these signs occur late and the diagnosis of pus formation should be made before they appear.

Once *pus has extended through the bone* into the subperiosteal space, local swelling, heat and redness are usually obvious, even in deep-seated bones. Extra-osseous as well as intra-osseous pus was present in three of our cases in this group (Table 3). In all of them there was visible swelling of the upper thigh, especially on the medial side and over Scarpa's triangle (Fig. 6a), extension of tenderness to the greater trochanter and upper femur (Fig. 6b) and increased muscle spasm which held the hip joint in some flexion, external rotation and abduction (Fig. 7). It should be noted that the duration of the illness in these cases varied from four to nine days and that in all of them the bone still contained pus under tension.

(2) SEPTICAEMIA—12 CASES. These children were all severely ill with fever of 103 to 107° F., tachycardia of 140 to 160, rigors or convulsions and often headache, drowsiness, delirium and epistaxis. In addition, symptoms such as flitting arthralgia, meningism, erythematous rashes, purpura, vomiting and diarrhoea tended to obscure the true diagnosis. Indeed, in two of the cases the patients also developed other lesions, namely pleurisy and pericarditis in one, and meningitis and pneumonia in the other.

In all the cases, the illness was of short duration (one to four days, with an average of 2·5), the leucocyte count was over 20,000 (22,000 to 45,000) and the sedimentation rate was over 80 mm. in the first hour (85 to 120). Blood cultures were positive in 10 cases; the two cases with negative cultures had received antibiotic therapy before admission.

The local signs were often not obvious, although intra-osseous pus was present in 11 of the 12 cases (Table 3). These severely ill patients do not complain of the excruciating local pain usually found in others, and the local lesion may be missed unless constantly kept in mind and specifically sought for. In six of the cases local tenderness over the neck of the femur was the only positive evidence of osteomyelitis and in five of them the presence of pus was diagnosed because the tenderness increased during the first 12 to 24 hours of antibiotic therapy. The sixth improved and was not operated upon. In the remaining six cases there was also evidence of swelling, local heat, etc., indicative of extra-osseous pus (Table 3), but in none were these signs very striking.

Not only are the local signs completely overshadowed by the general condition of the patient, but it is this type of case that tends to have multiple osseous lesions. Five of our patients had other

bones involved, namely tibia (two cases), opposite femoral neck, lower femur and ulna. In such cases the lesion in the deep-seated femoral neck is easily missed, and was in fact at first overlooked in two of our cases.

(3) SEVERE TOXAEMIA—FOUR CASES (FIVE BONES). All these patients had a long history (six to 18 days—average nine days). They were severely toxic with temperatures of 102 to 105° F. Leucocyte counts ranged from 18,000 to 63,000, and the sedimentation rate from 50 to 95. Blood culture was positive in one case only.

Local tenderness and swelling were well marked and extensive in all the cases. In two the swelling involved the whole thigh and fluctuation, indicative of pus in soft tissues, could be detected. Local heat, redness and dilated veins were equally prominent, and in two of the patients movements of the hip joint were markedly restricted, suggesting infection of the joint. In all these cases pus was found outside as well as inside the bone (Table 3), and in two of them the pus within the bone was still under tension.

Diagnosis

We did not accept the diagnosis of acute osteomyelitis as proven until one or both of the following criteria had been satisfied:

1. Pus in the bone as found at operation and confirmed by culture.
2. Radiological evidence of serial changes in the affected bone consistent with the presence of pyogenic infection.

Intra-osseous Pus. The femoral neck was explored in 26 cases (27 bones) and intra-osseous pus was found in 24 (25 bones, Table 3). In seven of these the pus was sterile on culture but all had received massive antibiotic therapy for long periods. On the other hand positive cultures were obtained in eight patients who had been on antibiotics for periods of three to 10 days.

In two cases only thin marrow fluid escaped and failed to reveal any growth on culture. Both presented with local pain and general inflammatory fever and on examination local tenderness was the only positive finding (Tables 2 and 3).

One patient who presented with septicaemia and minimal local signs which responded to conservative treatment, was not operated upon and it thus cannot be proven whether pus had yet been formed.

Radiological Changes. It is well known that radiological changes are conspicuous by their absence during the first 10 to 14 days of acute osteomyelitis. Radiographs are, therefore, valueless in assisting early diagnosis. Indeed, if treatment can be started at a really early stage of the disease, it may prevent altogether the appearance of radiologically detectable bone changes (Trueta and Morgan, 1954). This, however, is rare in hospital practice (Trueta and Morgan, 1954), and, as far as we are aware, we have not had the good fortune to encounter such a case.

All our patients, including the case not operated upon, developed radiological changes after two to three weeks. The earliest signs were usually a small area of erosion in the neck of the femur and minimal periosteal reaction (Fig. 8). In later cases decalcification, gross destruction of the femoral neck and sequestrum formation (Fig. 9) could be seen. Grossly neglected cases proceeded to involvement of the hip joint and destruction of the femoral head, giving the appearance of so-called Tom Smith's

FIG. 8.—Early radiological changes: slight erosion of femoral neck and minimal periosteal reaction.

FIG. 9.—Extensive erosion and sequestrum formation.

FIG. 10.—Gross destruction of femoral head and involvement of the hip joint: 'Tom Smith's arthritis'.

FIG. 11.—Involvement of the femoral shaft with extensive bone destruction and periosteal new bone formation.

arthritis (Fig. 10). (It is our belief that the majority of cases of Tom Smith's disease in patients over 2 years are in fact due to neglected osteomyelitis of the femoral neck.) In other late cases extension of the infection to the shaft of the femur may result in widespread destruction of bone, periosteal new bone formation and sequestration (Fig. 11).

Treatment

Our treatment of acute osteomyelitis is based on the following principles:

1. To combat the infection by adequate antibiotic therapy.
2. To provide rest.
3. To let out pus when it has formed.
4. To prevent complications.

Antibiotics. A great deal has been written on the value of antibacterial drugs in the treatment of acute osteomyelitis (Agerholm and Trueta, 1946; Higgins, Browne and Bodian, 1947; Dennison, 1952). The mortality of the disease has been reduced from about 25% without any drugs (Pyrah and Pain, 1933; McAdam, 1945; Higgins *et al.*, 1947; Dennison, 1948) to 10% with sulphonamides (Dennison 1948) and to 2 to 3% with penicillin (Altemeier and Helmsworth, 1945; McAdam, 1945; Stevenson, 1946).

There are, however, certain reservations and limitations in connexion with antibiotic therapy which are often overlooked:

1. It has repeatedly been shown that antibiotics will cure the blood infection, but that progressive bone destruction continues despite amelioration of the general symptoms (Agerholm and Trueta, 1946; Dennison, 1952; Du Plessis, 1953; Trueta and Morgan, 1954). It is well known that antibiotics cannot sterilize an abscess (Agerholm and Trueta, 1946), and we have now had a large number of cases, including eight with osteitis of the femoral neck, in whom pus, which contained viable organisms, was evacuated from the bone after intensive and prolonged antibiotic therapy.
2. Antibiotic therapy, to be effective, must be correct, intensive and prolonged.

Correct antibiotic therapy obviously depends on culture of the organism from the blood or the bone, and the result of this is usually not available for two to three days. Much has been written on the efficacy of penicillin. We agree that it gives excellent results provided the organism is penicillin-sensitive and have used it in 80% of our cases (66% of those with femoral neck involvement). However, in 20% of our cases the organisms have been insensitive to the drug and we, therefore, commence treatment with penicillin and one of the tetracycline group of drugs. (In desperately ill patients we prefer to use chloramphenicol or erythromycin and novobiocin because in 4% of our cases the organisms have been sensitive to these drugs only.)

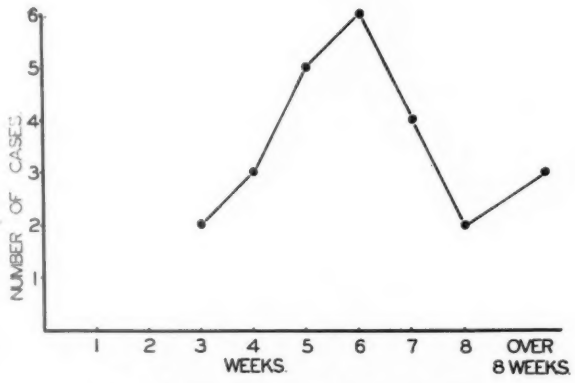


FIG. 12.—Duration of raised E.S.R. in 25 cases.

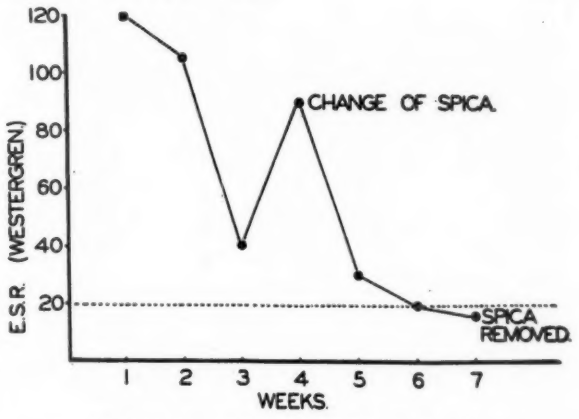


FIG. 13.—A typical chart of the weekly E.S.R. readings in an uncomplicated case. Note the effect of change of plaster.

Massive dosage is particularly important as far as penicillin is concerned. We now give 2-3 million units per day depending on age, commencing with six-hourly injections. (This is changed to oral penicillin when the temperature subsides.) Tetracyclines are given in dosages of 15 mg. per lb. per day.

Prolonged therapy is as important. Bitter experience has taught us that premature cessation of antibiotic treatment only too frequently leads to recrudescence or complications. We, therefore, continue not only until all general and local signs have completely subsided, but *until the sedimentation rate has dropped below 20 mm. in the first hour and remained there for at least a week*. The duration of treatment in our cases has ranged from three to eight weeks (average six weeks) in uncomplicated cases (Fig. 12), and we feel most strongly that anything less is inadequate and may be disastrous. (In three complicated cases therapy was continued for three to six months.)

Rest. A century ago John Hilton (1863) said: 'Rest is the necessary antecedent to the healthy accomplishment of both repair and growth. This surely is the natural suggestion of a means towards an end which should never be lost sight of by the physician or surgeon.'

The value of immobilization in the treatment of acute osteomyelitis is often overlooked. It is true that immobilization is usually mentioned but its purpose seems to be 'to prevent fractures and dislocations' rather than to provide the rest referred to by John Hilton.

We have found that inadequate or too brief a period of immobilization results in recrudescence of infection, and predisposes to complications. It has, therefore, become our policy to immobilize the bone in a plaster cast until the sedimentation rate has returned to normal. This index of activity has proved of great value (Fig. 12). First, it has been interesting to observe the effects of change of plaster, transport to a convalescent home and other movement on the sedimentation rate (Fig. 13). Second, in the past when we used to dispense with complete immobilization before the E.S.R. had returned to normal, our complication rate was almost twice as high as at present.

In the cases of osteitis of the femoral neck, this immobilization has been achieved by applying a plaster spica from waist to toes (Fig. 14). Plasters are changed at regular intervals and radiographs taken at the same time. Weekly sedimentation rates, leucocyte counts and haemoglobin estimations are carried out and recorded on a special chart. Complete immobilization is continued until clinically and radiologically there are no signs of activity and two successive E.S.R. readings are below 20 mm. in the first hour. The average period of immobilization has been six weeks with a range of three to

FIG. 14.—Adequate local rest is ensured by immobilization in a plaster spica from waist to toes.

FIG. 15.—Osteomyelitis of the left pubic ramus. An initial, erroneous diagnosis of osteomyelitis of the femoral neck was made.

eight weeks in uncomplicated cases. (The average period of hospitalization for all cases of osteomyelitis has been 45 days.)

Drainage of Pus. Our policy follows that of Trueta and his colleagues (Agerholm and Trueta, 1946; Trueta and Morgan, 1954), and is based on the age-old dictum that 'where there is pus it should be let out' and the belief that adequate drainage of bone *in patients over 2 years* can be obtained only by an open operation and drilling.

Our criteria for the diagnosis of intra-osseous pus have already been mentioned and have been well tested by an experience which we regard as unparalleled. The diagnosis of osteitis of the neck of the femur, however, is often extraordinarily difficult and mistakes have been made. These include:

1. Drilling of the bone before pus has formed. This happened twice in 26 cases (27 bones), i.e. in 7·4%. In both cases, operated upon early in the series, the local physical signs were merely tenderness and restricted movement, but the bones were drilled immediately instead of awaiting the result of a 24-hour trial of antibiotic therapy. Although no pus was found, subsequent radiographs proved the diagnosis to be correct.

It is possible that these cases would have recovered without surgery. On the other hand the drilling does not disturb the architecture of the bone and in both cases marrow fluid escaped under tension This tension is due to intramedullary oedema which tends to cut off the blood supply to adjacent areas and leads to thrombosis (Agerholm and Trueta 1946). It may, therefore, be argued that the decompression was actually beneficial and allowed the circulating penicillin to reach the site of the disease. Both patients have done very well, with complete bone healing and restoration of full function.

2. Drilling of the femoral neck because of mistaken diagnosis. This happened twice (the cases are obviously not included in the series). In one child, after a negative exploration, the temperature leucocytosis and sedimentation rate returned to normal within three days, and the patient was discharged after two weeks, perfectly fit. Subsequent radiographs revealed no bony changes and the correct diagnosis, in retrospect, was probably cellulitis. Another child, who also had a negative exploration, subsequently developed signs of osteitis of the pubic ramus (Fig. 15). In neither did the drilling procedure have any harmful effects.

It has been suggested that drilling is not necessary when pus has appeared under the periosteum. We cannot agree with this. Extra-osseous pus was present in 14 of our cases and in all of them pus was also found within the bone (Table 3). Indeed, in nine the intra-osseous pus was still under tension. This is in keeping with our overall experience, namely that the mere presence of pus outside the bone is not indicative of adequate decompression and that drilling is, therefore, necessary even when subperiosteal pus is found.

Our method consists of operating on the bone under general anaesthesia as soon as the patient is fit for surgery. In moderately ill patients who present with merely the usual general reaction to inflammation a few hours are profitably spent in rehydrating the patient and obtaining an adequate blood level of antibiotics. A delay of more than six to 12 hours is not regarded as justifiable, unless there is doubt about pus formation. If there is septicaemia it must first be overcome by intensive antibiotic therapy for 12 to 24 hours before surgery is undertaken. In neglected cases suffering from severe toxaemia due to the presence of a large abscess of long standing only slight improvement can be expected with antibiotic therapy, rehydration and blood transfusion and it is wise to operate as soon as the patient is considered fit for simple drainage of the abscess.

In the usual metaphyseal infection of long bones the standard approach is used to expose at least half the shaft of the affected bone which is then drilled in several places. In the case of the femoral

FIG. 16.—For drilling of the femoral neck the child is placed in the lateral position with a 45 degree backward tilt. Note the position of the scar.

neck the child is placed in the lateral position with the diseased side uppermost and with a 45-degree backward tilt (Fig. 16). When involvement of the hip joint is suspected, the joint is aspirated, using the lateral route. (The synovial fluid was turbid in two cases of this series, but in neither was pus obtained nor any growth on culture.)

The upper femoral shaft is approached through a lateral incision centred opposite the base of the greater trochanter (Fig. 16). Fascia lata, muscles and periosteum are incised and the periosteum elevated only just sufficiently to expose the bone. Subperiosteal pus, if present, is evacuated and a specimen taken for culture.

A small hole is drilled through the cortex of the femur at a point about 0·5 cm. below the base of the greater trochanter. A hand awl is passed up the middle of the neck of the femur, bearing in mind the angle of the neck to the shaft and its anterior rotation on the shaft (Fig. 17). The femoral neck is very short in children and since it is inadvisable to traverse the epiphyseal plate because of the risk of infecting the head of the femur and hip joint, the awl is inserted for not more than 1-1·5 in. Radiographic control is of great value and has been used as a routine; an antero-posterior radiograph usually suffices because the cortex of the superior and inferior limits of the femoral neck can be felt by gentle manipulation of the awl. In young children the awl will suffice to decompress the neck, but in older children the hole has to be enlarged with a $\frac{3}{16}$-in. drill. Pus usually escapes from the drill hole with some force and a specimen is taken for culture.

The upper shaft of the femur is drilled as well in case the infection has already spread. (Pus was found in six of our cases.) Drill holes are made at 1 cm. intervals until at least two fail to yield any pus (Fig. 18).

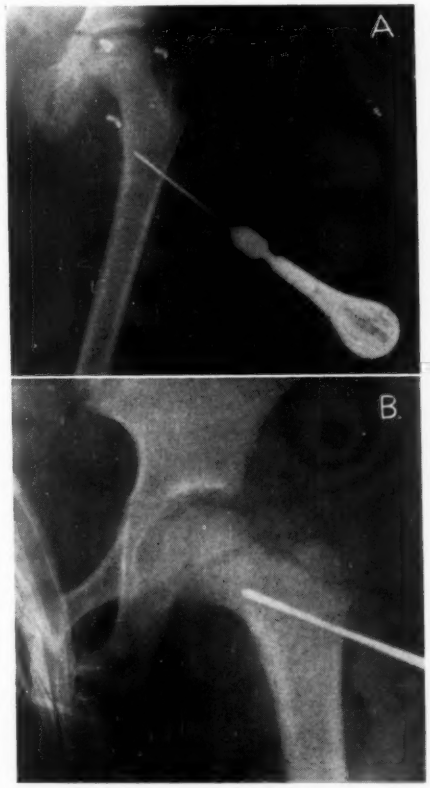


FIG. 17.—Radiographic control of decompression of the femoral neck. In (*a*) the direction of the awl is obviously incorrect, but this is easily adjusted by paying attention to the three skin clips and 'aiming' at the middle clip. In (*b*) the drill is correctly sited.

FIG. 18.—In this patient pus was found in the upper femoral shaft as well as in the neck of the femur. Note that the drill holes extend half-way down the shaft.

A corrugated rubber drain is inserted down to the bone and the wound is sutured. A plaster of paris spica is then applied from waist to toes (Fig. 14). On the fifth postoperative day a window is cut in the plaster over the wound under strictly aseptic conditions and the drain is removed. The window is replaced and securely closed and on the tenth day the sutures are similarly removed.

Prevention of Complications. When we are satisfied that all activity has ceased and there are no complications, antibiotic therapy and complete immobilization are discontinued and radiographs of the bone are taken. In some of the younger children who received treatment at an early stage the bones were sufficiently well calcified to render further protection unnecessary. In the majority including all those in the older age groups, there was still decalcification, and these patients were fitted with weight relieving calipers to prevent pathological fractures. They were followed up as out-patients and the calipers were removed when successive radiographs indicated adequate recalcification. Although the calipers, which were left on for an average period of six weeks, did not always achieve their original purpose, they did effectively limit the children's activity and prevent complications.

Results

The results of treatment are set out in Table 4.

Early. There have been no deaths. (Our overall mortality for acute osteomyelitis has been 1·5%, i.e. five deaths in 331 cases.)

Two patients (one with involvement of both femoral necks) are still under treatment and although both are doing well, it is still too early to assess the early results.

Of the remaining 25 cases, 24 were treated by medullary decompression. Three of these developed

TABLE 4

RESULTS OF TREATMENT

	Deaths (All Forms of Treatment)	Early Results (Drilling Only)	Late Results (2–7 yrs) (Drilling Only)
Osteitis of neck of femur (27 cases)* ..	—	Good 21 (87·5%) Complicated 3 (12·5%)	Full recovery 14 (82·5%) Unsatisfactory 3 (17·5%)
Osteitis in general (331 cases)	5 (1·5%)	Good 178 (88·2%) Complicated 24 (11·8%)	Full recovery 94 (86·2%) Unsatisfactory 15 (13·8%)

* One case treated conservatively: uncomplicated early but unsatisfactory late result. Two cases still under treatment.

immediate complications. Two had been ill for more than a week (eight and 10 days) and were profoundly toxic on admission. At operation large extra-osseous abscesses were found as well as intra-osseous pus under tension. Both developed septic arthritis of the hip joint after admission and required active treatment for six months; one also developed osteitis of the ulna. In the third patient, who had been ill for four days, surgery was delayed for three more days because of an error in diagnosis (the initial diagnosis was osteitis of the ilium). His illness was complicated by a protracted pyrexia for four weeks and the development of a sequestrum which gradually resorbed. He was discharged from hospital after three months with some limitation of movement of the hip joint.

In 22 cases the immediate results were excellent (21 were operated upon and one was treated conservatively). None developed metastatic foci, joint involvement, pathological fractures or dislocations, sequestra or recurrence after apparent recovery. Temperatures returned to normal after an average period of five days (one to 14 days). All the wounds healed by primary intention. The sedimentation rates reverted to normal after three to eight weeks (average six weeks) and a normal range of movement was re-established in all.

In summary, therefore, complications occurred in 12·5% of the surgically treated cases. This corresponds with our overall experience in cases treated by medullary decompression. In 202 cases of acute osteomyelitis of various bones so treated 11·8% developed complications (Shandling, 1960). These results compare favourably with those of others who adopt a similar line of treatment (Agerholm and Trueta, 1946; Dennison, 1952; Du Plessis, 1953; Trueta and Morgan, 1954). It should be mentioned that in the past, before we inserted drains as a routine after drilling, early wound complications, such as serous collections and temporary sinuses, were twice as common as at present. In this connexion it should be noted that in Trueta and Morgan's (1954) series 50% of the patients developed a temporary sinus which 'occasionally appeared some time after the stitches had been removed'.

In contrast to these results, we found that in 67 of our cases who were treated entirely conservatively or by simple drainage of extra-osseous pus, early complications occurred in 35%. This is in keeping with the findings of some (Agerholm and Trueta, 1946; Dennison, 1952), although at variance with those of others (Caldwell and Wickstrom, 1950; Altemeier and Largen, 1952).

Late. Eighteen of the patients have been followed up for seven years to two years. Among them are included the three patients who had early complications. Two of these have developed subluxation of the hip joint with marked limitation of movement, gross irregularity and thickening of the neck and shaft of the femur and considerable shortening. These two results are obviously bad, but there has been no recent recrudescence nor sequestrum formation. The third patient (who developed a sequestrum that resorbed) has slight limitation of movement of the hip joint, shortening of the limb and, on radiograph, widening, irregularity and patchy destruction of the neck and upper shaft of the femur.

A fourth case, ironically the patient who was treated conservatively, also has an unsatisfactory result. Clinically there is a slight limp and minimal limitation of hip joint movement, but the radiographs show patchy destruction of the neck and upper shaft of the femur.

In the remaining 14 cases (82·5% of those treated surgically) the results have been excellent. All the children have returned to normal activity with full restoration of hip joint function, complete bone healing and non-adherent scars (Fig. 19). Increased growth in length and width of the femur is present in six cases (Fig. 20), but does not exceed 2 cm. There have been no sinuses, no pathological fractures, no sequestra and no late recurrences.

These late results are somewhat less satisfactory than our overall results in acute osteomyelitis, in which 86·2% of the cases followed up for one to seven years, have recovered completely with 100% normal function (Shandling, 1960), and not as good as those of Trueta and Morgan (1954) who obtained full function in 94% of their cases. However, allowance must be made for the following three factors:

1. The age of the patients. Trueta and Morgan (1954) have found that the age of the patient has a well-marked effect on the end result of osteomyelitis. 'The structure of the bone needs several years to revert to its normal pattern and the intensity of this reversion is progressively lost in approaching the final stages of growth.' Since half our patients were aged 10 to 12 years, the age factor may account for the comparatively long periods (six weeks) of hospitalization. Furthermore, the ages of the patients who developed complications and imperfect healing were 9, 10 and 12 years.

2. The lateness of the diagnosis. The average duration of illness in our cases of osteomyelitis of the femoral neck was six days. In the two cases with the worst results the duration on admission was eight days and 10 days. In a third case who

FIG. 19.—Late result in 82·5% of the cases, full function restored, scars well healed and non-adherent.

had been ill for four days, we were responsible for a further delay of three days before operating. (The fourth case with a poor result was treated conservatively and is not considered.)

Early diagnosis is undoubtedly one of the most important factors in the successful treatment of osteomyelitis and this may be excessively difficult in osteitis of the femoral neck. It is obviously a problem not only for the surgeon, but also for the general practitioner and paediatrician, and the disease must be given pride of place in the clinical consciousness of all of us.

FIG. 20.—Late result, complete healing of the femur with slight increased growth in length and in width.

3. The operations were performed by different surgeons (mainly registrars) and this unavoidably introduced a variable personal factor in the technique and thus also a small variation in the results.

Conclusion

In general our results compare favourably with those of others who have been treating acute osteomyelitis by medullary decompression (White and Dennison, 1952; Trueta and Morgan, 1954). Good results with conservative treatment have been claimed by some (Caldwell and Wickstrom, 1950; Altemeier and Largen, 1952), but these workers include in their series many cases without radiological signs of osteitis. Since these patients were not operated upon, the grounds for the diagnosis of osteomyelitis must be questioned, and the presence of bone infection cannot be accepted as proven. In our own experience and also in that of others (Agerholm and Trueta, 1946; Dennison, 1952), the results of conservative treatment leave much to be desired.

As far as osteomyelitis of the neck of the femur is concerned, too little has been written for comparison, but, judging from the numerous reports in the literature on septic arthritis of the hip joint with destruction of the head and neck of the femur, it is our impression that osteitis of the femoral neck has frequently been overlooked in the early stages only to be followed by this disastrous com-

p ication which is then regarded as the primary le ion.

While fully realizing that a good number of our ca es have not yet reached the end of their evolution, w are convinced that the results of metaphyseal decompression are superior to those of conservative treatment, and feel justified in continuing our method of treatment, particularly in acute osteomyelitis of the neck of the femur. There is no room for complacency, however, and our objective should be 100% satisfactory results. To achieve this, early diagnosis, as always, is at a premium and can be made possible only if every practitioner, paediatrician and surgeon is constantly aware of the possibility of acute osteomyelitis and sufficiently alert to detect the early signs of the disease.

We would like to express our indebtedness to our colleagues and registrars who treated many of these patients; particularly to Mr. Arnold Katz who is in charge of our Osteitis Ward. Professor A. Kipps and Dr. D. McKenzie and their respective Bacteriological Departments have co-operated to the full at all times, and thanks are also due to the Medical Superintendents of the Red Cross War Memorial Children's Hospital and Groote Schuur Hospital for access to the case records. Finally, we wish to thank Mr. G. McManus, Miss R. E. Malan and Mrs. P. Kottler for their help with the photography and preparation of the manuscript.

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RECURRENT URINARY INFECTION IN GIRLS*

BY

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It is a commonplace that recurrent and persistent urinary infection result from stasis in the urinary tract, and it is the elimination of major obstructions which has proved the worth of urological surgery. This paper is concerned with those children, almost always girls, who suffer recurrent infections, yet whose urinary tracts show no obvious sign of stasis, and in whom the intravenous pyelogram shows no significant evidence of obstruction. During the past few years our approach to these cases has altered somewhat: at first we were inclined to treat them largely by continuous chemotherapy and even if this treatment did not prevent recurrences in all cases it was believed that attacks usually ceased spontaneously in the end, often at the age of puberty. The danger in this approach, however, is that with each attack of pyelonephritis, destruction and scarring of the renal parenchyma becomes more extensive, and that, although symptoms of urinary infection may disappear, loss of renal substance may be severe and precipitate renal failure much later in life, particularly if infection is reactivated, as often occurs during pregnancy. In recent years, therefore, we have tried to assess the extent of this pyelonephritic scarring from radiological data, and to determine whether any minor disorders of lower urinary function could be rendering the child liable to recurrent infection. Such disorders are mild bladder neck or urethral obstruction, producing only some trabeculation but no more than a small volume of residual urine, and vesico-ureteric reflux occurring on micturition, uncomplicated by serious dilatation of the ureters. Bladder neck obstruction in girls has in fact been diagnosed much more often during the past three years than in the earlier period, and only in the past 12 months have we undertaken regular surgical treatment in cases of reflux.

Results of Conservative Treatment

Our first approach has been a retrospective survey of all cases of recurrent urinary infection seen in The Hospital for Sick Children, Great Ormond Street, during the six-year period 1951-56. Only those who had had urological investigations and who had been considered at the time to have no urinary tract disorder were selected for follow-up. Of a large number of cases reviewed, therefore, only 102 were selected for further consideration and all these patients were asked specifically whether they had suffered from further attacks of urinary infection, and, if so, whether they would be prepared to submit themselves to further urological investigations. The results of the survey are set out in a table (Fig. 1). It will be seen that 24 patients were finally reinvestigated and assessed and that 15 of them had normal urinary tracts.

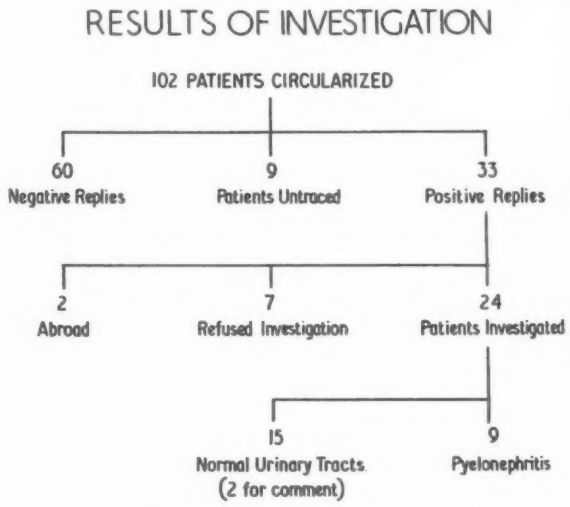

FIG. 1.—Table showing the result of a survey of 102 girls with recurrent urinary infection.

Clearly these figures have no statistical significance in estimating the incidence of serious complications after urinary infection; the survey was not wide enough and the material too highly selected, but they do give us some idea of what is happening to our patients. None of these girls has proved to have a progressive type of bladder

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July, 1960.

neck obstruction and none of those cystoscoped, because of recurrence of symptoms, had trabeculation. It does appear therefore that in our original series we had not overlooked any serious obstruction. By contrast, progressive pyelonephritic scarring has been observed in several, and on re-examining the original films we now consider that at least some signs of scarring were present at the first investigations.

Chronic Pyelonephritis

The radiological signs of chronic pyelonephritis have been admirably described by Hodson (1959), and his findings have been amply confirmed in this series. This author has also drawn attention to the association of pyelonephritic atrophy with vesico-ureteric reflux, to which we will allude later. In the diagnosis of chronic pyelonephritic lesions it is essential to see not only the pyelogram, but also the renal outline: where ordinary films do not reveal this the stomach can be distended with a fizzy drink; alternatively, tomography may be used. A nephrogram can also be obtained by giving an intravenous injection of hypaque while the ureter is blocked by a tight ureteric catheter, or even by aortography. The characteristic sign of pyelonephritic atrophy (Figs. 5 and 7) is an irregular loss of renal substance; the renal outline is indented and approaches close to the calyx, which is usually blunted. Often this narrowing is confined to one pole of the kidney, though such a finding may well underestimate the pathological extent of the lesion. In the differential diagnosis of pyelonephritis with contraction, two other conditions must be borne in mind: first, foetal lobulation, which is usually evident in the early months of postnatal life, but may persist for longer; indentation of the renal outline is then observed, but it is not associated with any narrowing of the renal substance and the indentations bear no relation to the normal calyx. Second, contraction of the whole kidney relative to its fellow, but with a smooth and regular outline, may be seen in renal artery stenosis causing hypertension, and may then be entirely unassociated with pyelonephritis. In advanced atrophy due to any condition, the pelvi-calyceal system is also deformed, so that a diagnosis may be made on simple pyelography; calyces are clubbed and closely packed together and the pelvis is relatively dilated, although without the cut-off seen on the obstructive hydronephrosis. Often the whole kidney seems compressed alongside the vertebral column, the pelvis and the ureter lying in the same straight line.

Pyelonephritic scarring may be static or progressive: progress may be accompanied by evident clinical infection or be entirely silent, with an insidious loss of renal substance. The following cases illustrate these points.

Case 1. J.B., aged 6 years, was first investigated in 1952 for persistent urinary infection of six months duration. The intravenous pyelogram at this time (Fig. 2) was thought to be normal, but on closer inspection it is evident that the left kidney is small with a regular outline and there is some irregularity of the calyces to the upper pole. Pyelography was repeated during this survey in 1959 (Fig. 3) and this showed a small, grossly contracted and pyelonephritic left kidney. Vesico-ureteric reflux was demonstrated on the left side.

FIG. 2.—Intravenous pyelogram (1952). Small left kidney with irregular upper calyx.

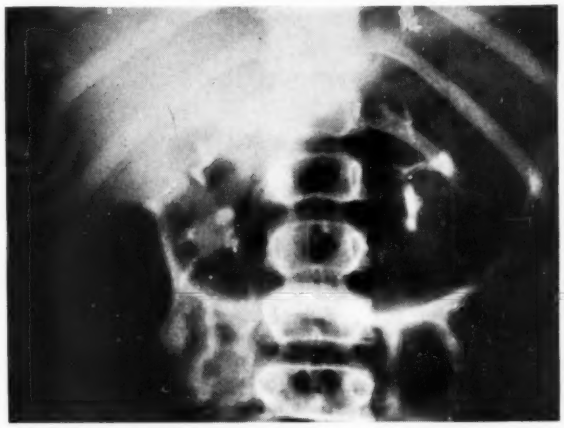

FIG. 3.—Intravenous pyelogram (1959) on the same patient as in Fig. 2. Grossly pyelonephritic changes of the whole of the left kidney.

She had remained perfectly well for seven years apart from one attack of urinary infection with pain in the left loin in 1954. This is a good example of a relatively symptomless progression of the pyelonephritic lesion.

FIG. 4.—Intravenous pyelogram (1954). Note clubbed calyx and thinning of the renal cortex of the upper pole right kidney.

FIG. 5.—Intravenous pyelogram (1959) on the same patient as in Fig. 4. Pyelonephritic scarring of the upper one-half of the right kidney.

Case 2. S.L.G. had an intravenous pyelogram performed in 1954 (Fig. 4) and this shows clubbing of the upper calyx of the right kidney with thinning of the renal cortex in this region. At the time these changes were not thought to be significant. Further pyelography in 1959 (Fig. 5) showed that the lesion had progressed to a considerable degree. The patient also demonstrated vesico-ureteric reflux on the right side. During the 12 months before the second investigation she suffered nine attacks of severe urinary infection. Earlier this year (1960) a Hutch procedure was performed to eliminate reflux on the affected side and she has been well since the operation.

Case 3. S.N. had three complete urological surveys between 1952 and 1959, but on each occasion the intravenous pyelogram did not satisfactorily demonstrate the right kidney, although it was suspected that this kidney might be the source of her repeated urinary infections. In 1959 an aortogram was performed (Fig. 6) and this demonstrated a nephrogram of a small contracted right kidney. Right nephrectomy was performed and the patient has remained well since her operation.

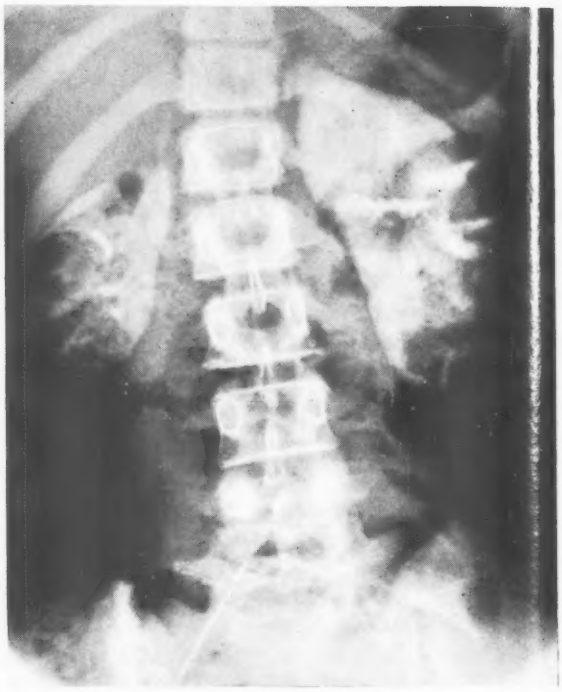

FIG. 6.—Aortogram of a pyelonephritic right kidney, confirmed at nephrectomy. (Reproduced by kind permission of Dr. C. J. Hodson.)

Case 4. J.R., aged 19 years, recently married, developed a urinary tract infection which was thought to be a 'honeymoon pyelitis'. She had had a full urological investigation in 1951 with negative result. An intravenous pyelogram (Fig. 7) made last year (1959) showed extensive pyelonephritic scarring of the upper one-half of the right kidney. A micturating cystogram demonstrated no vesico-ureteric reflux. This progression of the pyelonephritis had been entirely symptomless. Earlier this year (1960) a partial nephrectomy of the upper one-half of the right kidney was performed. At operation there appeared to be well-localized disease of the upper pole of the right kidney.

Pyelonephritic scarring is the result of infection and what we are really seeking is the cause. It is true that the renal lesion itself sometimes seems responsible for the perpetuation of the infective process, so that excision of the damaged element is the only useful treatment, but we hope to find,

in an increasing proportion of affected children, a curable lesion in the urinary tract, so that renal tissue may be preserved wherever possible.

Bladder Neck Obstruction

Until two or three years ago, we were very reluctant to make this diagnosis in the female child: we encountered a few cases with a grossly sacculated bladder which appeared to be obstructed, but might also have been neuropathic; but by contrast with many urologists in the United States, we did not recognize many examples of mild bladder neck obstruction. It was suspected that the practice of transurethral resection made for sloppy diagnosis in this respect; it is too easy to say that there is just a little obstruction which can be treated by just a little resection, whereas if an open operation is required the criteria are apt to be a little stricter. Moreover, the fact that in adult practice very few young women are seen with any degree of bladder neck obstruction, mild or severe, made it seem unlikely that we were missing many mild cases in childhood. However, adult women are commonly afflicted by so-called idiopathic chronic pyelonephritis, accentuated during pregnancy and causing renal failure. Some of these cases do show vesicoureteric reflux and slight trabeculation of the bladder, suggesting therefore that a mild obstruction is present or has been present at some stage in their evolution. It seems possible, therefore, that in the female we might be dealing with a disease process whose natural history differs from the better recognized male cases of bladder neck obstruction progressing to severe hydronephrosis.

FIG. 7.—Intravenous pyelogram (1959) of a 19-year-old woman. Pyelonephritis of the upper pole of the right kidney. Partial nephrectomy performed.

We have therefore been on the look-out for cases of mild obstruction in girls and during the past two years we have made the diagnosis on 28 occasions, though open operation has been performed on only 24 and it is this smaller group only which will be considered. Twenty of the 24 had suffered recurrent or persistent attacks of urinary infection, usually on a very large number of occasions with severe temperatures, and resisting long periods of chemotherapy. Many of the girls with infection also had enuresis, but two had enuresis with sterile urine, one complained only of frequency and one only of loin pain. The age of presentation varied from 4 to 18, with a very considerable preponderance of the 6 to 10 age group.

Physical examination gave very little information and of course spinal cord lesions were excluded. A residual urine was definitely present in 19, it was sufficiently large to produce a palpable bladder in five but small volumes varying from 20 ml. to 200 ml. were present in fourteen. Intravenous pyelograms were reported in the first instance to show slight ureteric dilatation in eight cases, and pyelonephritis unaccompanied by dilatation in three. Thirteen of the children were studied by cineradiology during micturition and eight more had good micturating cystograms with still pictures. These cystograms have been analysed for four factors: the presence or absence of sacculation of the bladder, residual urine, reflux and the form of the urethra.

Sacculation in the form of two or three small pouches behind the ureteric orifices had been present in many of the cases with trabeculated, thickened bladders. They have not been seen in the simple enuretics who are as near to normal controls as we have been able to get for cineradiology. We regard the presence of saccules as highly suggestive of an obstruction, but not absolutely diagnostic.

A residue in the bladder at the end of an uninhibited micturition was counted as definite evidence

FIG. 8a.—Retrograde pyelograms showing moderate dilatation of the ureters and pyelonephritic scarring of the kidneys in a child aged 3 years with the bladder neck obstruction syndrome.

FIG. 8b.—Micturating cystogram in the same child, showing very considerable dilatation of the ureters during the act of micturition.

of obstruction, and it could often be recognized in the radiographs, particularly in the cine films. There are obvious pitfalls provided by the frightened child who will not perform properly, and by the return of urine which has refluxed into the ureters during bladder contraction, though this latter is usually distinguishable on the cine film.

Reflux was present in eight and absent in 13; it was therefore present much less often than residual urine and was in fact often unilateral. Only those with good micturating films have been included in this count since reflux is found more often during micturition than on a simple filling cystogram. Although reflux appeared to be more common in the obstructed bladder than in the non-obstructed, and experience with the male cases certainly corroborates this, we do not regard reflux alone as evidence of obstruction, since it can obviously be due to local abnormalities in the ureteric orifice.

Reflux, then, has many causes, but it is a relatively common complication of bladder neck obstruction in girls. It has, however, definite associations in the upper urinary tract; when unilateral it occurs on the site of the worse kidney whether this is hydronephrotic or contracted with pyelonephritis. In intravenous pyelograms the ureters often appear atonic with slight and inconstant dilatations; during micturition, at the height of the bladder contraction, they are considerably dilated (Fig. 8).

Many of the urethrograms have an unusual appearance which has not been satisfactorily explained. The bladder neck appears as a ring-like constriction; the urethra below it may be a tube of uniform calibre, but may show a dilatation tapering at the lower end rather like a spinning top (Fig. 9). This is marked when the bladder contraction is forceful and is accentuated if an attempt is made to restrain micturition. At first it seemed to suggest an obstruction in the lower urethra, but we have not been able to demonstrate such an obstruction either on endoscopy or exploration. Moreover, the dilatation tapers at the lower end; it does not bulge as does the posterior urethral outline in valvular obstruction in boys, nor does the urethra stay full after micturition as it does behind the other obstructions. It is suggested that once micturition has begun and the hypertrophied bladder is contracting forcefully, the bladder neck is no longer a severe obstruction so that the powerful stream distends the thin walled urethra below the internal sphincter.

On cystoscopy the cardinal feature has been

trabeculation indicating detrusor hypertrophy, and it is upon the presence of trabeculation that we have relied in the diagnosis of those mild cases without residual urine. It may be difficult to judge the limits of normal in respect of trabeculation and one must be careful to avoid an over-distended bladder or an inadequately anaesthetized and straining child. It is a subjective observation in which experience is of great importance; it has been misjudged on at least one occasion recently, and the bladder at operation was not found to be hypertrophied; this case was therefore excluded from the bladder neck obstruction category. The bladder neck may appear as a prominent ring through the right-angle cystoscope and it usually does so through the urethroscope. It closes down promptly as this instrument is withdrawn down the urethra.

The operation performed has been a Y-V plasty in 23 cases and a simple myotomy in one. The upper part of the bladder has been opened as well in order to assess the detrusor hypertrophy present in all cases included in this series. The bladder neck can be felt as a hypertrophied ring, but it is slack so that it will admit the finger, whereas a normal one often will not. When incised longitudinally the hypertrophied ring is evident, but the urethra below it is thin walled and capacious. Histologically there has been no evidence of the urethral-fibroelastosis which Bodian (1957) found in some boys with Marion's disease. We do not know the exact nature of the pathology therefore; some features do suggest a lower urethral obstruction but we are calling these cases bladder neck obstruction simply because the muscle around the bladder neck is hypertrophied and we have not found a distal obstruction. Moreover, operations on the bladder neck lead to an improvement.

FIG 9.—Micturating cystogram in a child of 7 years with the syndrome of bladder neck obstruction, showing a trabeculated bladder, a saccule on the right side and the tapering dilatation of the urethra below the bladder neck.

This brings us to an analysis of the results; of 14 cases of recurrent infection with more than six months' follow-up, 12 have remained sterile. The two who recurred have both got severe bilateral reflux. One case with simple frequency has been relieved, also one with loin pain alone. Enuresis alone was present in two; one is relieved, the other is not. In general the continence has been much better after the operation than it was before, though some of the cases with recurrent infection who have sterile urine now are still wet at night.

The conclusions drawn from this series are as follows: among the girls who suffer recurrent infections without gross deformity of the urinary tract are some with a mild degree of obstruction which in the absence of clearly defined pathological evidence we label bladder neck obstruction. It differs from the disease seen in the male in that progression to retention and hydronephrosis is uncommon, but it predisposes to infection and chronic pyelonephritis. In the diagnosis true residual urine is of great significance, as is unquestionable trabeculation of the bladder: a micturating cystogram should always be performed to detect complicating reflux. Y-V plasty is a satisfactory treatment in the majority, but may fail to relieve the condition where reflux is severe.

Reflux

Reflux has already been discussed as a complication of bladder neck obstruction, but has many other causes. It is also seen in association with hypoplastic kidneys, double ureters and other malformations, or it may be due to local abnormalities such as vesical diverticula encroaching upon the ureteric orifice. In this study of recurrent infections in girls where pyelograms do not show any gross abnormality a further condition, the megacystis syndrome, requires mention. Large non-trabeculated, thin-walled bladders associated with lax ureteric orifices and bilateral reflux have been described by Marcel (1952) and more recently by Paquin, Marshall and McGovern (1960). The

cases of mega-ureter—megacystis syndrome previously described by one of us (Williams, 1954) appear to be severe examples of the same disease, and several cases without mega-ureter have now been investigated. In the past we have been inclined to treat these conservatively, as Marcel has done; more recently we have undertaken operations to prevent reflux as Paquin *et al.* advocate. Comparative results are not yet available, however, and will not be discussed here.

Reflux unassociated with any identifiable bladder abnormality has also been encountered in cases of recurrent urinary infection: whether it is the cause or the result of an inflammatory process is not yet apparent. Once again surgical treatment is being tried and will be reported later.

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ENDEMIC URINARY LITHIASIS IN TURKISH CHILDREN*†

A CLINICAL STUDY OF 119 CASES

BY

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Endemic urinary lithiasis is a clinical entity with the following characteristics: a high prevalence in boys, a high percentage of bladder stones, uric acid as the usual chemical constituent of the stones, restriction to the lower social and economic classes, a well-marked peak incidence of the disease between 2 and 4 years and a limitation to certain parts of the world.

Civiale (1838) was one of the first to report an extensive series of cases. In Great Britain the disease was common at the end of the last century but disappeared dramatically between 1910 and 1920 (Lett, 1936; Thomas, 1949). Assendelft (1900) reported a series from Russia, Bokay (1912) from Hungary, Račić (1935) from Yugoslavia and Balacesco (1929) from Roumania. Chevalier (1929) and Brown and Brown (1941) reported cases from Syria, Levy and Falk (1957) from Israel and Brun (1933) from Tunisia. The disease has also been reported from China (Thomson, 1921), from Siam (Noble, 1931) and from India (McCarrison, 1931).

Erkun (1935), Taner (1940) and Ozdilek (1946) have reported previous series from Turkey where the disease appears to be commoner than anywhere else.

Whereas detailed analyses of sporadic urinary lithiasis in childhood have been published by Myers (1957) and by Winkel Smith (1944) from Great Britain and Denmark respectively, no such analysis appears to exist for the endemic form of the disease and no extensive series has been reported in the British literature for almost 30 years.

Present Investigation

The series under review covers 119 consecutive cases of urinary lithiasis in children which were seen and diagnosed at the Hacettepe Children's Hospital in Ankara between January 1958 and May 1960, a period of two years and four months. The Hacettepe Children's Hospital is a new children's hospital which is part of Ankara University's Medical School and it is unlikely that any selection of patients has taken place in this series. The steadily increasing number of lithiasis patients seen is in proportion to the increasing number of all surgical cases seen during the time of this study. During the same period about 42,500 new patients were seen in the hospital's out-patient departments and about 6,000 patients were admitted. Urinary lithiasis cases therefore represent approximately one in 350 patients seen and one in 51 patients admitted to the hospital. Operations for calculus disease have accounted for 9% of all surgical procedures carried out by us.

The patients came from all parts of Turkey, but the majority were from the Anatolian plateau; relatively few came from the fertile coastal districts as is shown on the map (Fig. 1). With very few exceptions our patients came from the lower social and economic classes; their fathers being either smallholders or labourers. In no instance was a family history of lithiasis elicited.

The anatomical distribution of the stones is shown in Table 1. Bladder and urethral stones thus accounted for 58%, while stones in the upper urinary tract were present in 42% of patients.

TABLE 1
ANATOMICAL DISTRIBUTION OF STONES

Site	Numbers	%
Kidney ..	41 (5)	30
Ureter ..	17 (3)	12
Bladder ..	55 (1)	42
Urethra ..	21 (1)	16
Total ..	134	

Figures in parentheses denote female patients.

In 23 patients (19%) the stones were in multiple sites (Table 2).

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

† Part of this material has been used in the thesis of M.D. of Cambridge University.

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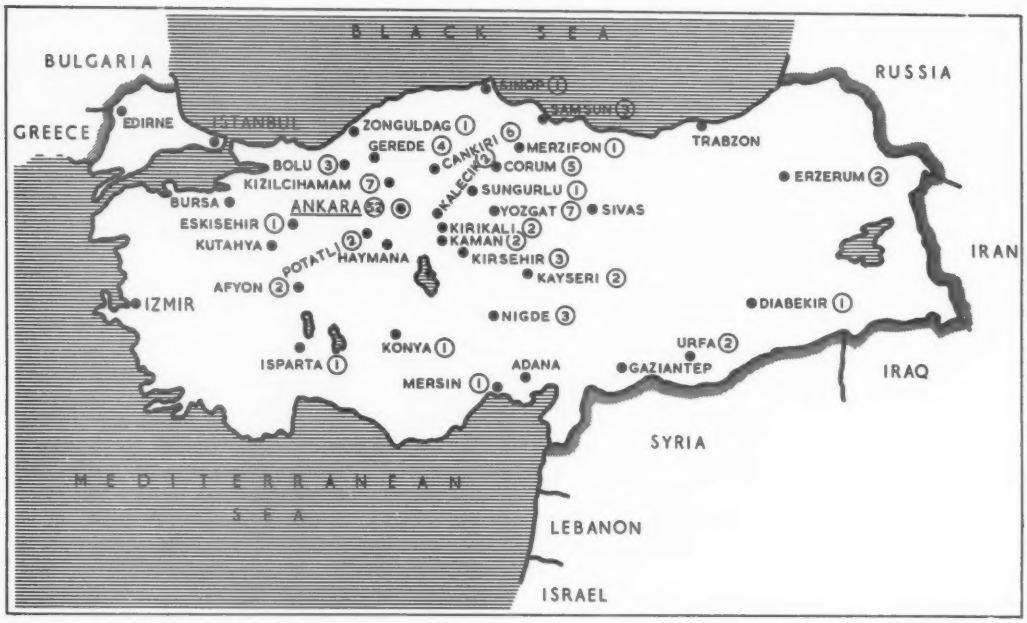

FIG. 1.—Map of Turkey showing incidence of stones. The circled figures indicate number of cases.

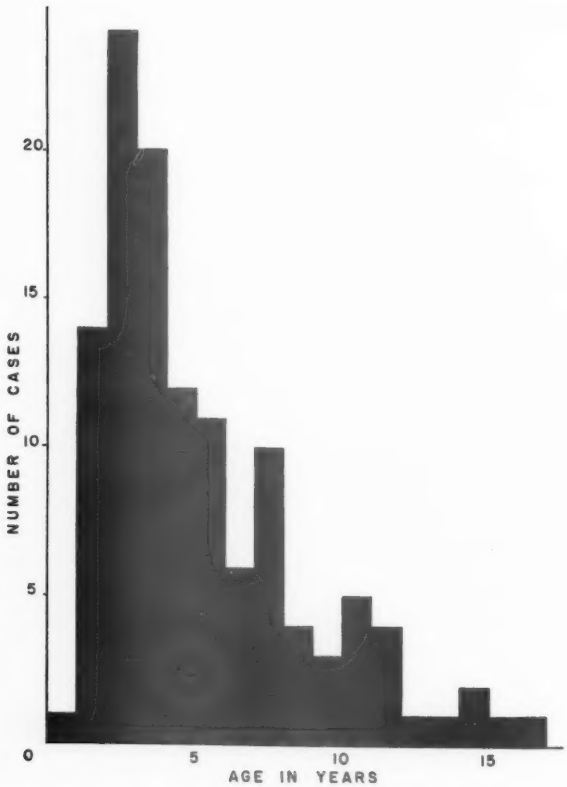

FIG. 2.—Age distribution of patients.

TABLE 2
DISTRIBUTION OF STONES IN MULTIPLE SITES

Multiple Sites	No. of Stones
Both kidneys	8
Bladder and kidney	6
Bladder and ureter	2
Bladder and urethra	1
Urethra and kidney	1
Urethra and ureter	2
Kidney and ureter	1
Urethra, ureter and kidney	1
Both kidneys and both ureters	1
Total	23

TABLE 3
SIDE OF KIDNEY OR URETER INVOLVED

	Kidney	Ureter
Left	18	7
Right	14	9
Bilateral	9	1

TABLE 4
PRESENTING SYMPTOMS

Symptom	Nos.
Dysuria	55
Abdominal pain	20
Retention of urine	11
Haematuria	10
Passing stones	5
Pyrexia	5
Anuria	3
Oedema	1
Ascites (abdominal swelling)	1
No symptoms	7

Although kidney stones were often multiple, stones in the bladder were almost always solitary.

The side affected in cases of upper urinary tract disease is shown in Table 3.

The age distribution of the patients is shown in Fig. 2. This shows a well-marked peak incidence between the ages of 2 and 4 years. However, when the cases are broken down into the different anatomical sites of the stone it becomes clear that the marked peak incidence applies only to stones in the bladder and urethra, while cases with upper urinary tract stones are evenly distributed throughout the years (Fig. 3).

There were 10 girls in this series (8·5%); five with kidney stones, three with ureteric stones and one each with a bladder and a urethral stone.

The presenting symptoms were recorded in 108 of the patients and are shown in Table 4. No fewer than seven patients had no symptoms referable to the stone, this being a chance finding during investigations for unrelated medical conditions. In eight of the children symptoms began while the child was still being breast fed.

The laboratory investigations carried out on the first 100 cases are shown in Figs. 4, 5 and 6. These show that the majority of the patients had normal haemoglobin values and that the non-protein-nitrogen (N.P.N.) was within normal limits in most of the uncomplicated cases. The serum calcium, phosphorus and alkaline phosphatase were usually normal. The urine was acid in about 75% of cases, but in some of these the reaction changed to alkaline

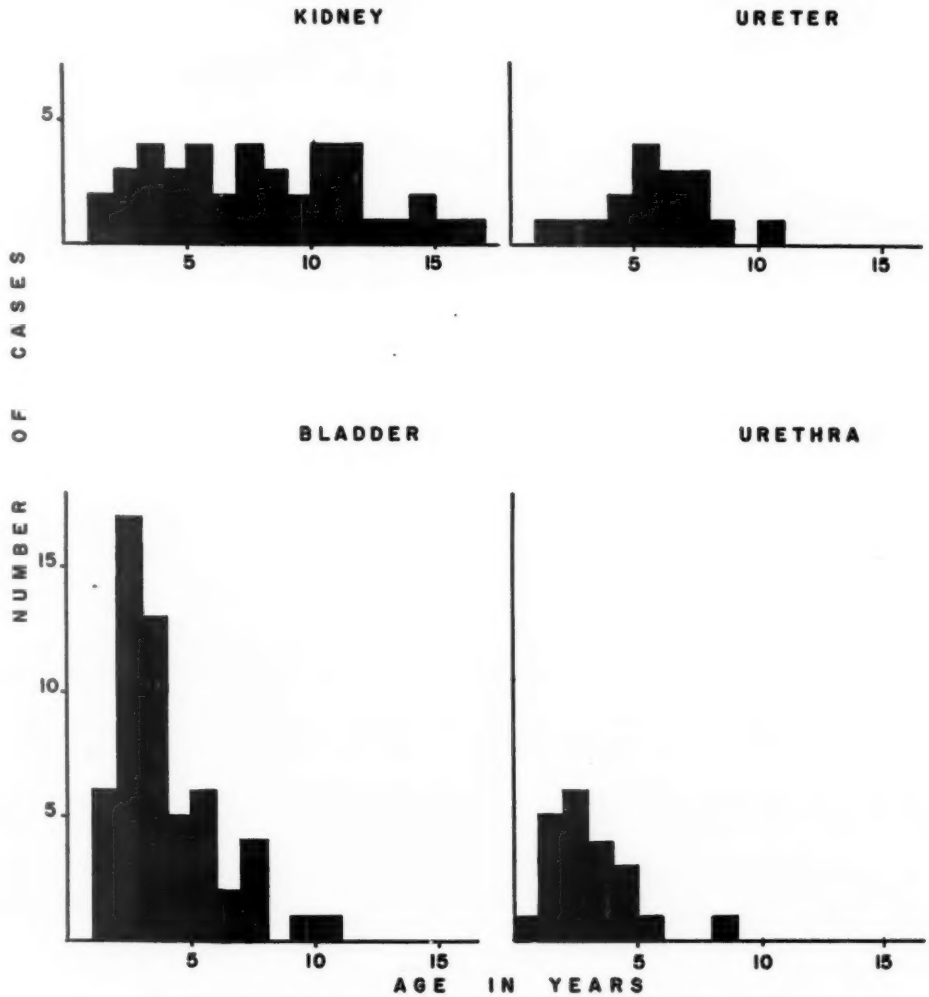

FIG. 3.—Cases broken down into different anatomical sites of the stone.

on repeated examinations. However, the *p*H of the urine at the time the stone is diagnosed may not be closely related to that at the time of stone formation. Microscopy of the urine usually showed epithelial cells, leucocytes and crystals of uric acid or oxalates.

All patients had an abdominal radiograph and in only four of these were the stones not opaque to X rays. We have made a point of using a large enough film to include the whole abdomen in all cases; in a number of these a silent kidney stone was found when the symptoms were referable to a bladder stone. Excretion urograms were carried out in 70 of the patients and in all but two of the cases the diagnosis was made or confirmed radiologically. Ureteric catheters were not available during most of this study.

The complications which were encountered are shown in Table 5. It will be seen that no less than 72 patients (61%) had a complication which could be attributed directly to the stone. Urinary infection was present in 25 patients and the organisms isolated from the urine are shown in Table 6. The more unusual complications encountered have been reported on previous occasions (Eckstein, 1960a; Eckstein, Oral and Dogramaci, 1958; Eckstein, 1960b; Eckstein, Marulyali and Tatman, 1959; Eckstein and Kenanoglu, 1961).

The treatment of the patients is summarized in Table 7. It has been our policy to remove all stones which were considered to be too large to be passed spontaneously (Campbell, 1951; Williams, 1958). Only two patients were suitable for conservative therapy, one case of ureteric stone and one of bladder stone and in six cases the spontaneous expulsion of a urethral stone occurred. In three patients no treatment was advised because of other disease (metastatic neuroblastoma of orbit, encephalitis and osteomyelitis with rheumatic carditis). In 78 patients (66%) surgical removal of the stone was carried out. Several children had more than one operation and a total of 98 surgical procedures was performed (Table 8).

We have not carried out instrumental removal of

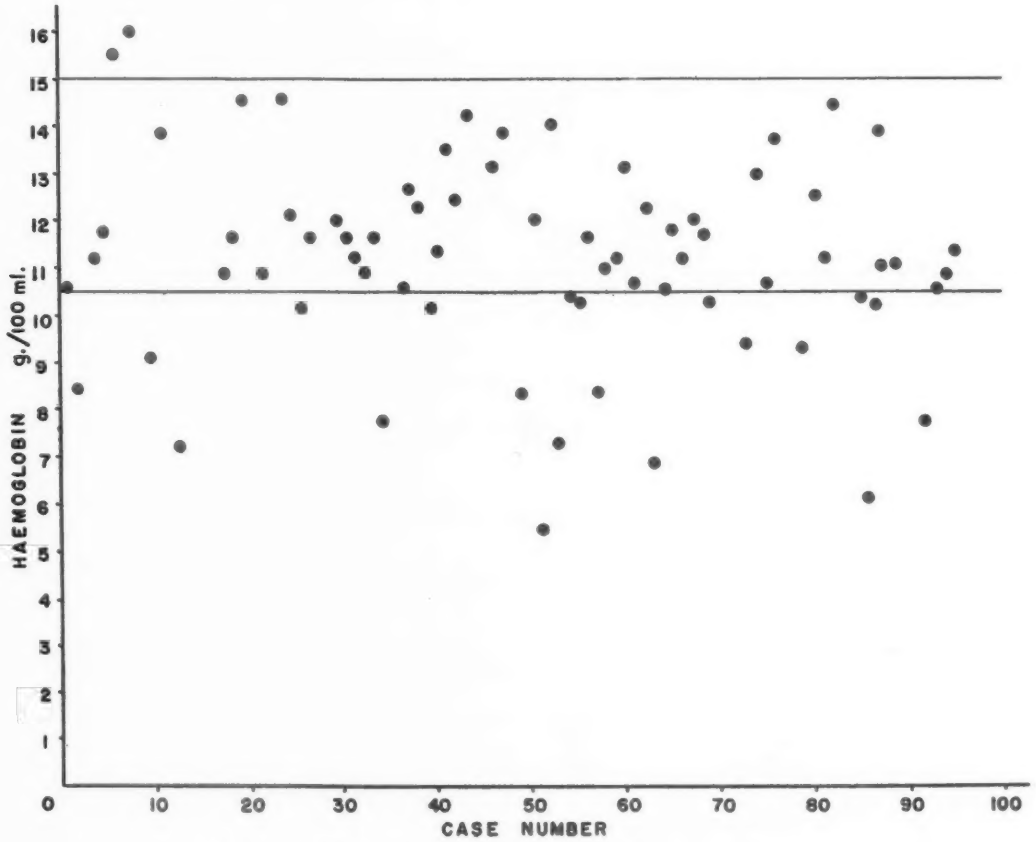

FIG. 4—Haemoglobin levels in first 100 cases.

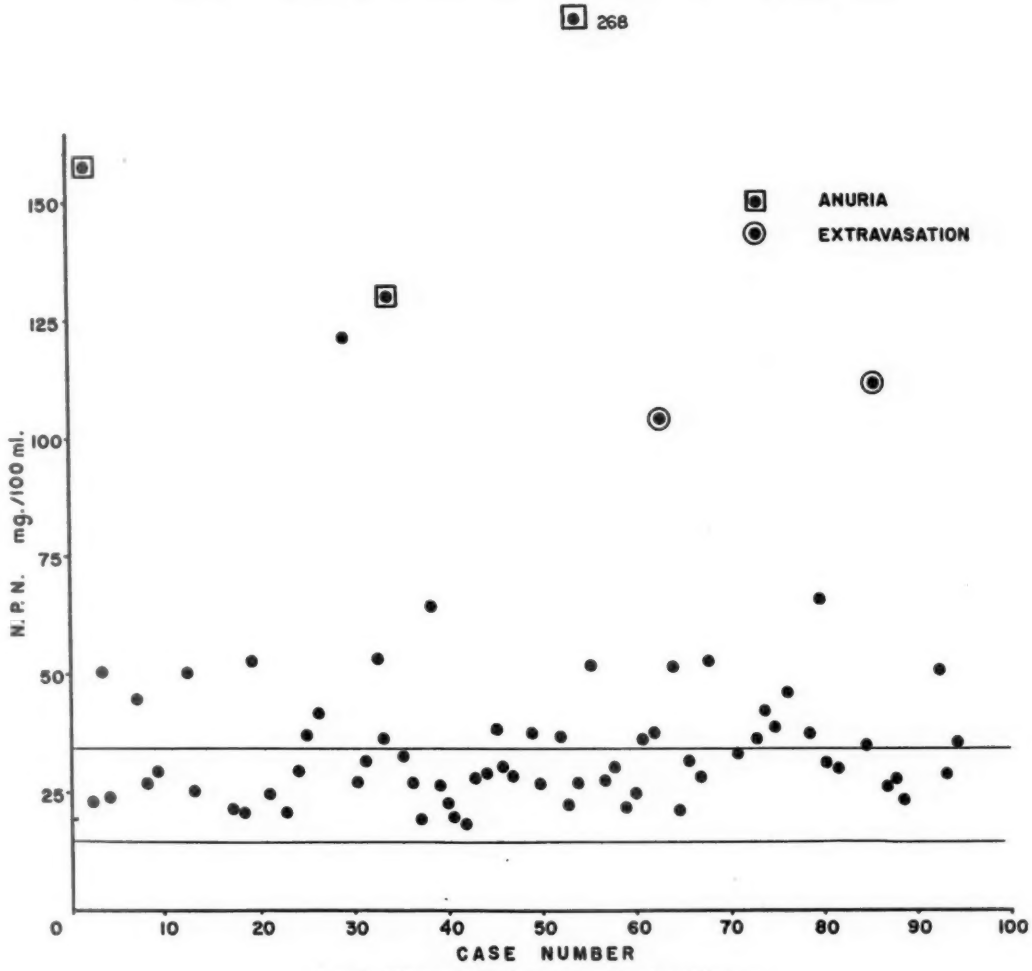

FIG. 5.—Non-protein-nitrogen levels in first 100 cases.

ureteric calculi nor performed lithotrity and agree with Grob (1957) and most other writers that, in children, surgical removal of the stone is to be preferred. Only Keegan (1900) and Winsbury-White (1954) advocate litholapaxy in boys. Impacted

TABLE 5
COMPLICATIONS

Complication	Nos.
Urinary infection	25
Hydronephrosis	21
Retention of urine	12
Pyonephrosis	4
Anuria	3 (1)
Extravasation of urine	2 (1)
Renal atrophy	2
Ureteric stricture	1
Perinephric abscess	1
Chronic renal insufficiency	1
Total	72

Figures in parentheses denote fatal outcome.

TABLE 6
URINARY INFECTIONS

Organism	Nos.
E. coli	12
Proteus	10
A. aerogenes	3
Ps. pyocyanea	2

TABLE 7
TREATMENT OF PATIENTS

Treatment	No. of Patients
Cases operated on	78 (66%)
Conservative treatment	2
Spontaneous expulsion (urethra)	6
No treatment (concomitant disease)	3
Referred for surgery elsewhere	7
Refused treatment	23 (19%)
Total	119

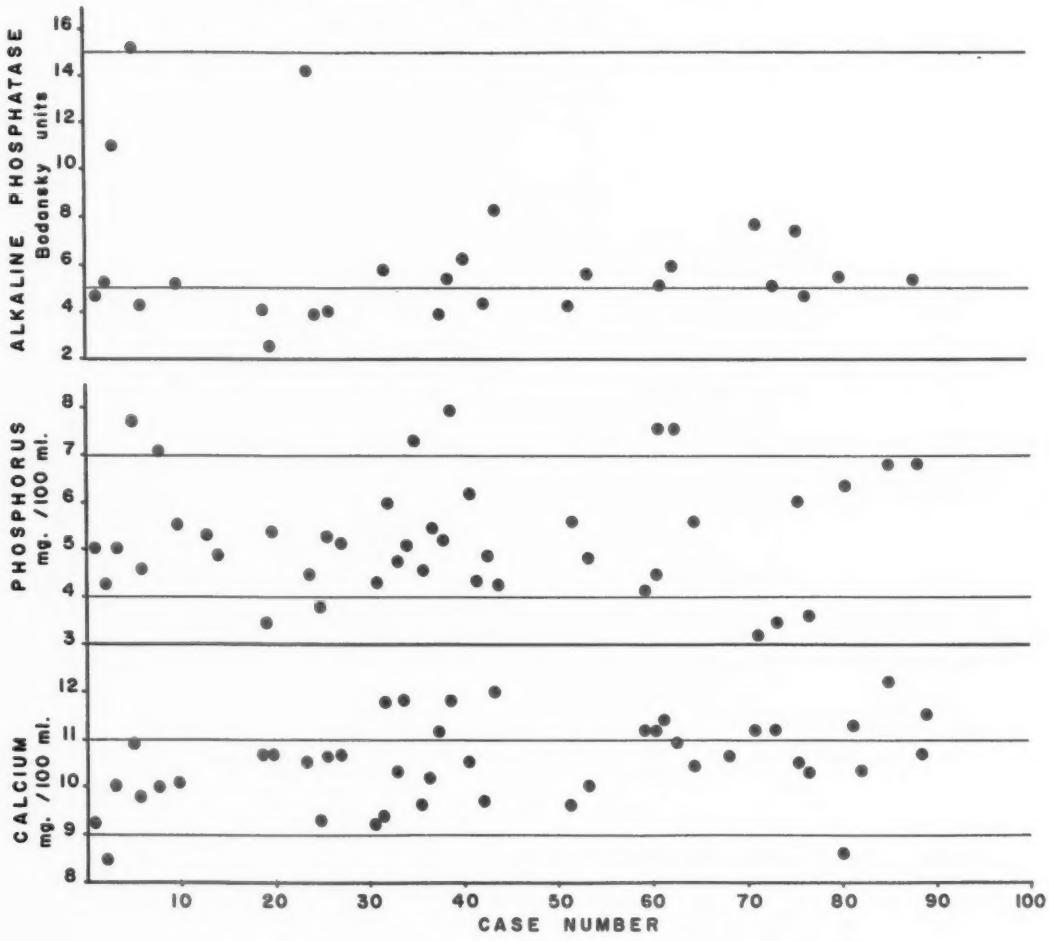

FIG. 6.—Calcium, phosphorus, and alkaline phosphatase levels in first 100 cases.

TABLE 8
SURGICAL TREATMENT

Treatment	Nos.
Bladder:	
Cystotomy	37
Cystoscopy only	1
Urethra:	
Cystotomy	4
Perineal urethrotomy	5
Stone extracted	4
Suprapubic drainage	3
Kidney:	
Pyelotomy	20
Nephrotomy	7
Nephrectomy	7
Partial nephrectomy	3
Nephrostomy	1
Ureter:	
Ureterolithotomy	5
Ureteroneocystostomy	1
Total	98

urethral calculi were removed by urethrotomy unless extraction with forceps could be carried out without traumatizing the urethra.

One child suffering from calculus anuria and one with perforation of the urethra and extravasation of urine died and there were two further deaths, probably from septicaemia, after simple cystolithotomy. There have been very few postoperative complications although one child required nephrectomy for secondary haemorrhage after pyelolithotomy.

The stones showed considerable variations in size and shape and were usually laminated. Fifty of the stones removed were analysed qualitatively and the chemical findings are summarized in Fig. 7 and in Table 9. Thus uric acid was present in 38 of the stones while phosphates and carbonates were uncommon findings. There was no significant

TABLE 9
CHEMICAL COMPOSITION OF STONES

Composition	No. of Stones
Uric acid only	18
Calcium oxalate only	7
Uric acid and calcium oxalate	15
Mixed (phosphates and carbonates)	10
Total	50

difference in the chemical composition of bladder and kidney stones. Epprecht and Schinz (1950) have shown that the uric acid in the endemic type of stone is present as ammonium urate and as a mixture of two forms of calcium urate.

Although an adequate follow-up study has unfortunately not been possible in our cases it is my impression that recurrences in the endemic form of urinary lithiasis are very uncommon.

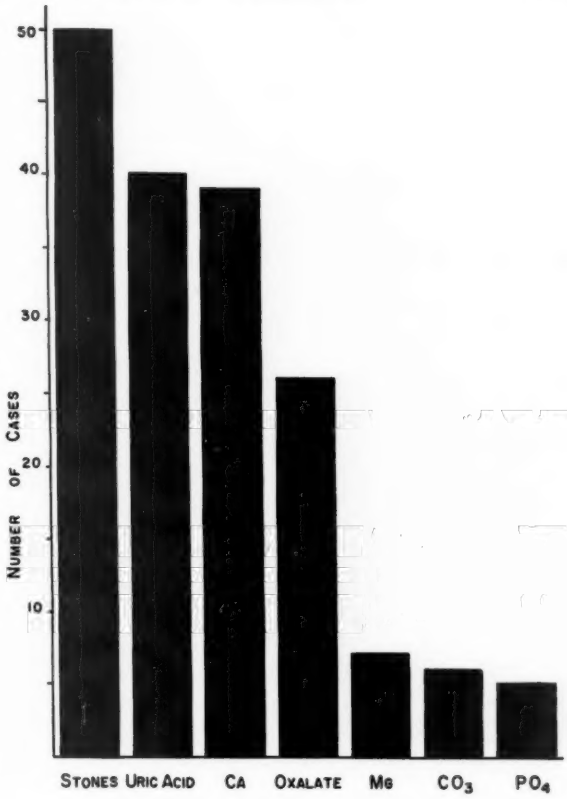

FIG. 7.—Chemical composition of stones.

Discussion

We have been unable, as yet, to carry out any complex biochemical studies to elicit the cause of endemic urinary lithiasis. However, the diet of Turkish children appears to be grossly deficient in protein and in vitamin D. Turkish children are breast fed much longer than British children and details about breast feeding are available in 45 of our cases. No less than 44 of these were breast fed, 28 (61%) for one year or more. Generally speaking cow's milk is not consumed by the village population and eggs and meat are eaten on rare occasions only. The staple diet is 'bulgur', a boiled wheat product, vegetables and fruit. Although rickets are very common in Turkey it has been an unusual finding in our cases suggesting that a vitamin D deficiency is not involved in the aetiology. Malnutrition is common in Turkish children and Dogramaci and Wray (1958) have shown that 41% of unselected out-patients were malnourished. The weights of our patients under the age of 6 years have been plotted on a graph produced from figures given by Gomez, Galvan, Cravioto and Frenk (1955) from Mexico where the standard of living is, to some extent, comparable with that in Turkey (Fig. 8). This shows that malnutrition is no more frequently seen in cases of urinary lithiasis than in the average hospital population. Severe vitamin A or C deficiencies are extremely rare and it is likely that a protein deficiency is closely related to the aetiology of endemic urinary lithiasis.

The incidence of upper urinary tract stones in this series is higher than in most of the previous ones reported in the past. Improved radiological facilities no doubt account for some of this difference, but probably some other factor is involved. Two recent reports on endemic lithiasis from Italy (Montinari and Torraco, 1956) and from India (Anderson, 1959) also quote an incidence of upper urinary tract stones of about 50%.

The male predominance has, in the past, been explained by the fact that the female urethra being shorter and wider than that of the male allows small stones to pass which would be held up in a boy's urethra. This theory may apply to bladder and urethral stones but cannot account for the similar sex difference in cases of upper urinary tract stones. It is therefore possible that a sex hormone is in some way involved in the complex aetiology of endemic urinary calculus formation.

The fact that the disease has disappeared in Great Britain within living memory, that it is virtually restricted to the lower social and economic classes and that it is at present endemic in those countries with a relatively low standard of living, especially where the lower social classes are concerned, strongly suggests that endemic urinary lithiasis can be prevented by an improved standard of living. It is possible therefore that this interesting condition

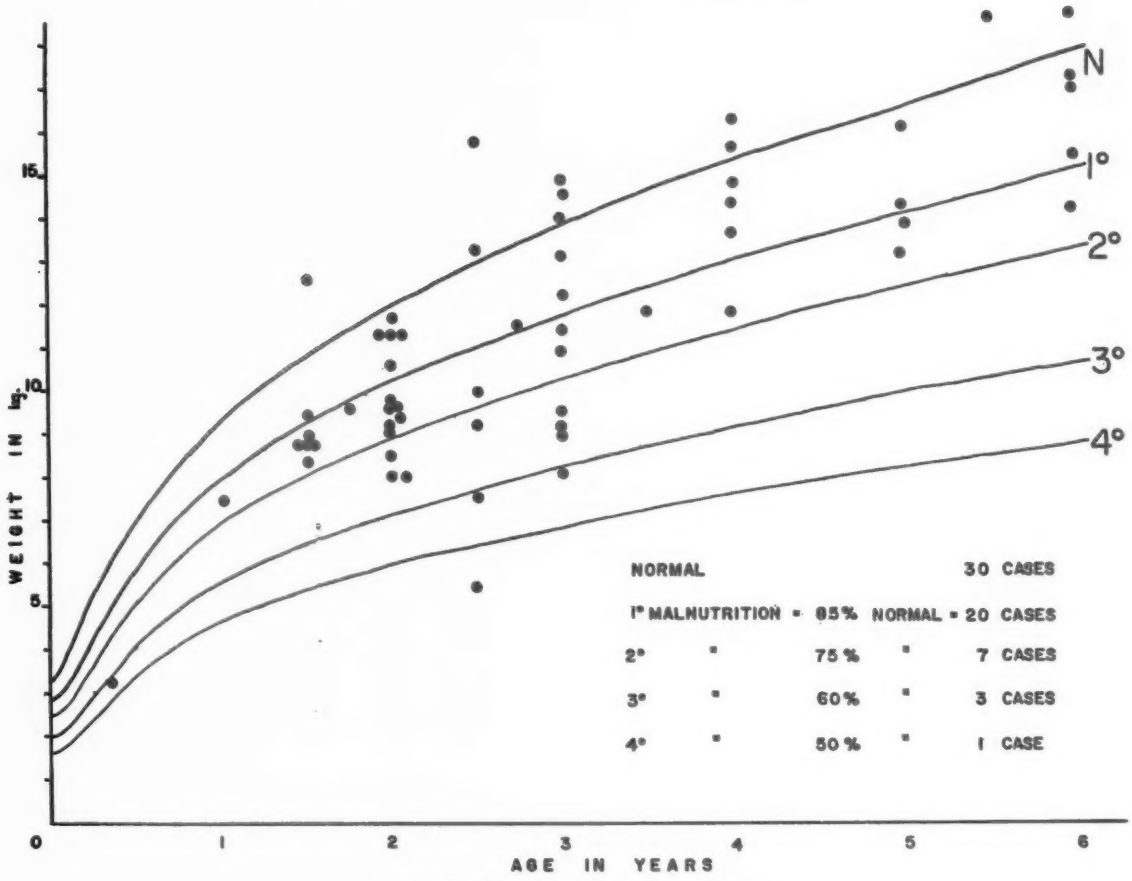

FIG. 8.—Weight of patients under 6 years of age.

will disappear before we have been able to work out its aetiological mechanism.

Summary

Endemic urinary lithiasis is a clinical entity with certain well-defined characteristics. A series of 119 consecutive cases which were seen at the Hacettepe Children's Hospital in Ankara have been reported and discussed. The aetiology of the disease is not known, but it is likely that a protein deficiency is the most important factor in a complex mechanism of stone formation. As the standard of living rises the disease will probably disappear.

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CONGENITAL ABNORMALITIES OF THE ANUS AND RECTUM*

BY

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This paper is based on a study I have made with John Partridge, until recently Resident Assistant Surgeon at The Hospital for Sick Children, of 323 cases of anorectal abnormality seen here in the 10-year period January 1949 to December 1958.

We feel that the most important fact with regard to treatment and prognosis in these cases is whether the bowel terminates above or below the pelvic floor. We accordingly make a primary distinction between high and low abnormalities. In the low abnormalities the bowel passes through a normal puborectalis sling and pelvic floor, and continence is assured even in the presence of an abnormal external sphincter. Treatment is therefore easier and less prolonged than in the high cases where there is usually an abnormal pelvic floor and deficient internal and external sphincter mechanisms.

The low abnormalities are subdivided into:

(1) The covered anus;
(2) The ectopic anus;
(3) The stenosed anus;
(4) Anorectal membrane.

1. *The covered anus* is common in males and rare in females. The embryological explanation of this deformity is that the anus is covered by excessive posterior fusion of the genital folds. On examination there is usually a $\wedge$-shaped bar of skin at the expected site of the anus, or the midline perineal raphe is thickened and may contain a meconium-filled track leading back to the anal canal (Fig. 1). In this and succeeding Figures the important rectopubalis muscle is diagrammatically represented. If both these distinguishing characteristics are absent diagnosis must be made from the common high anomaly.

2. *The ectopic anus* is common in females and rare in males and results from defective migration of the embryonic bowel. According to the site at which the bowel terminates below the pelvic floor this group is divided into the vaginal, the vestibular, the vulval and the perineal ectopic anus (Figs. 2, 3 and 4).

3. *The stenosed anus* may be easily visible but reduced in calibre or it may be of pin-hole size (the microscopic anus described by Denis Browne), and here I would like to say how many of our ideas concerning these low abnormalities have resulted from the work of Denis Browne (1951) and Douglas Stephens (1953a, b). Embryologically this abnormality is caused by excessive fusion of the anal tubercles.

We have also included in this category the less usual type where the stenosis occurs within the anal canal at the level of the anal valves. This is due to incomplete breakdown of the anal membrane. Should this membrane remain imperforate our fourth division results.

4. *Anal membrane* (Fig. 5) is a rare anomaly. It has been confused with the covered anus when the covering is very thin, and sometimes with Hirschsprung's disease when withdrawal of the examining finger is followed by a gush of meconium.

The high anomalies are subdivided into:

(1) Anorectal agenesis,
with or without fistula;
(2) Rectal atresia;
(3) Cloaca;
(4) Multiple abnormalities,
e.g. ectopia cloacae.

1. *Anorectal agenesis* is more common in the male than the female and in over 75% of our male cases there has been an associated fistula into the prostatic urethra (Fig. 6). We have not encountered a rectovesical fistula.

2. *Rectal atresia* (Fig. 7) has previously also been known as the Ladd type IV anomaly or imperforate rectum; the anal canal ends blindly below the pelvic floor and the upper rectal pouch ends at or above this level.

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

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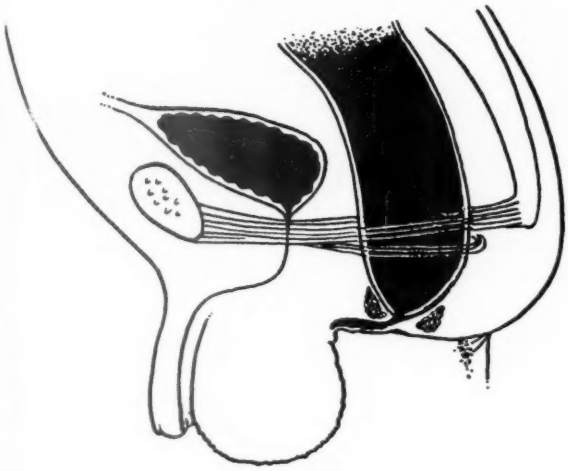

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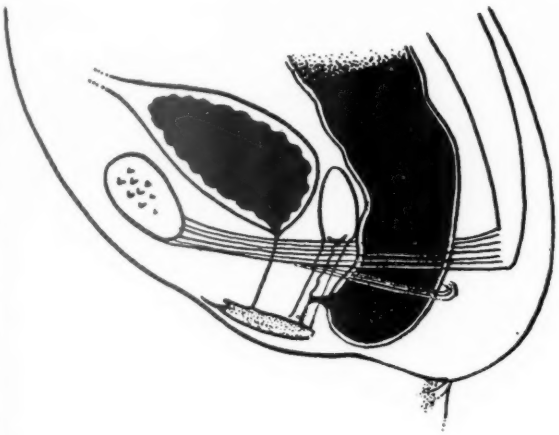

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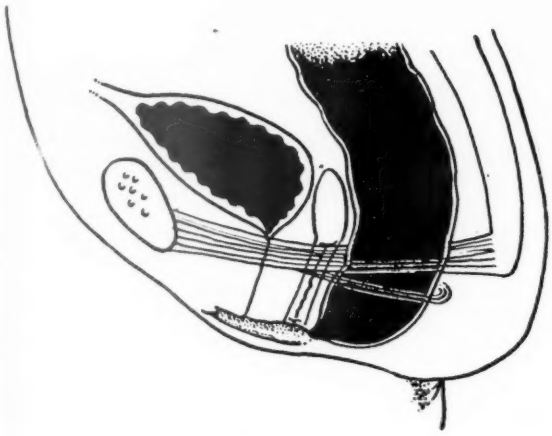

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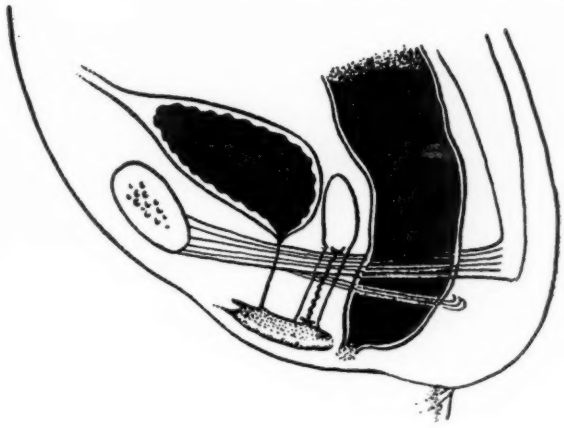

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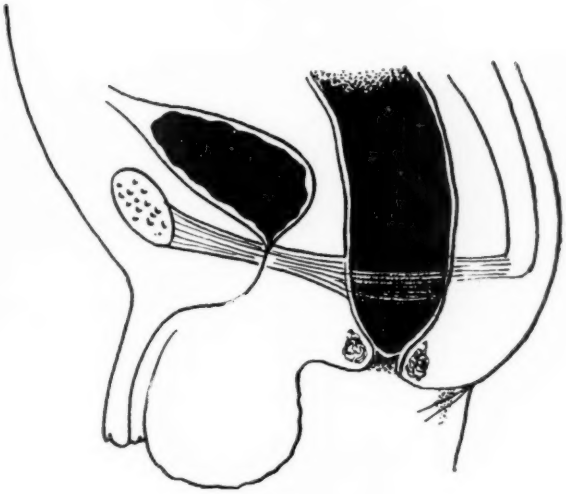

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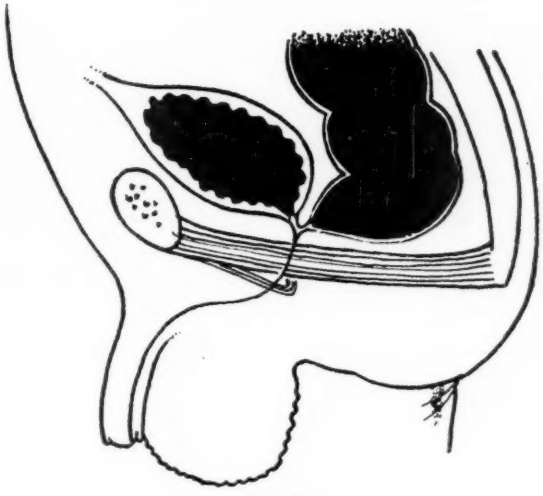

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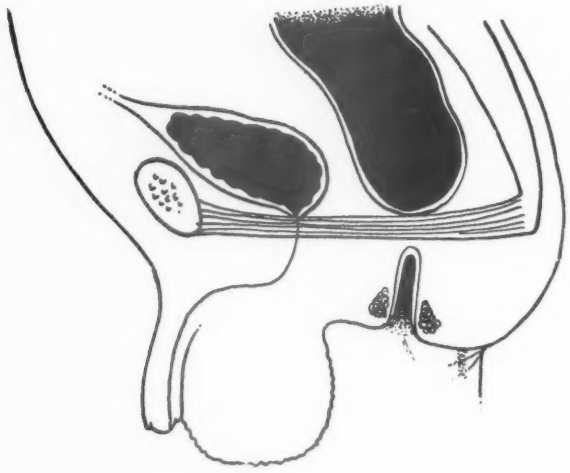

FIG. 7.

We have been accused of bandying words in applying the term agenesis to the first abnormality and atresia to this. Following the definition of these words in the Shorter Oxford Dictionary (3rd edition, reprinted in 1955) we have used agenesis to indicate imperfect development of the functional unit (as it is used in renal agenesis) and atresia to indicate occlusion (as in duodenal atresia). We have avoided using the term 'imperforate anus', which at times has been used to describe the whole group of anomalies and at others to describe certain types within this group. We have also reserved the term 'fistula' for use in the description of high anomalies, using 'anus' to describe the ectopic or abnormal termination of the bowel in the low abnormalities. We hope that this will stimulate the idea that a low ectopic opening can be encouraged to function as an anus, whereas this is not the case with the fistula in the high cases.

3. *Cloaca* (Figs. 8 and 9) is used to describe the anomaly in females when the urinary, genital and alimentary tracts all open into a common wide cavity (Gough, 1959).

4. Our fourth heading, *Multiple abnormalities*, includes ectopia cloacae (vesico-intestinal fissure) and other severe malformations.

Incidence

Of the total number of 323 cases, 60%, or 192, were low anomalies and 40%, or 131, were high; 57% of the children were males.

Table 1 shows the numbers of each type of the low anomaly. The common male anomaly is the covered anus, and the common female anomalies are the perineal, vulval and vestibular ectopic anuses.

Stenosed anus is more common in the male (29 of the 38 cases); the figures stress again the relative infrequency of the anal membrane.

FIG. 8.

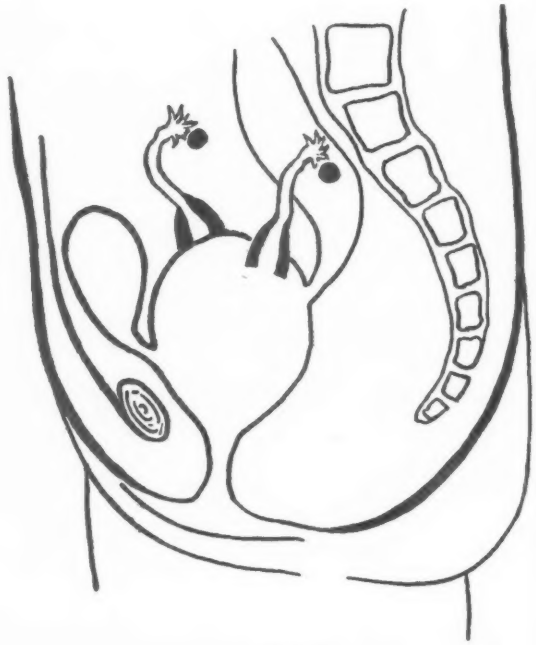

FIG. 9.

TABLE 1
INCIDENCE OF LOW ANOMALIES

Low Anomaly		No. of Cases
Covered anus		53
Ectopic anus		98
perineal and vulval	57	
vestibular	33	
vaginal	8	
Stenosed anus		38
Anal membrane		3
Total		192

TABLE 2
INCIDENCE OF HIGH ANOMALIES

High Anomaly		No. of Cases
Anorectal agenesis		114
male	103	
female	11	
Rectal atresia		5
Cloaca		9
Multiple abnormalities, e.g. ectopia cloacae		3
Total		131

Table 2 shows the incidence of the high anomalies and among these the great majority were anorectal agenesis in the male.

Our findings also confirm the high incidence of associated congenital abnormalities; 64% of the high and 25% of the low anomalies had other, often multiple abnormalities. The commonest associations were of skeletal, cardiac and genito-urinary malformations and we now consider that all these children should have an intravenous pyelogram performed. In the absence of urinary infection we prefer to delay this investigation until 1 year of age; the radiographs are more satisfactory then and the radiation risk is diminished. We have regarded the presence of a fistula in the high cases as part of the anomaly rather than an associated anomaly.

Treatment and Results

Low Abnormalities. The covered anus has been treated by the cutback operation described by Browne (1951) or if there has been no track, the anus has been uncovered by excision of a circle of skin. The perineal and vulval ectopic anuses have been similarly treated by cutback; the vestibular ectopic anus has been treated by dilation only, by cutback or by transplantation. We now favour transplantation. The vaginal ectopic anus has been either transplanted or pulled through by the abdomino-perineal method. Treatment of the stenosed anus has been dilation, and of the anal membrane, rupture and dilatation. Some children were referred having been treated initially elsewhere; many of these were sent for advice about colonic inertia (which used to be known as acquired megacolon), which had developed secondarily to stenosis of the anus, and long periods of bowel re-education have been required.

The results of treatment are shown in Table 3. Under the heading of the anomaly the total number of cases is repeated, followed by the number of children who have died; the third column represents children who cannot be traced, or for whom there is inadequate follow-up, and the fourth column therefore gives the number available for study; this is followed by the division of results into good, fair or poor. A *good* result indicates normal bowel control without regular laxatives; *fair* indicates the need for continual supervision to avoid recurrent constipation or anal stenosis; these children usually are being maintained on laxatives and suppositories, and *poor* indicates that a state of incontinence or severe colonic inertia still exists. In the final column we have inserted the average length of follow-up; this, with the fair and poor results gives some idea of the anomalies which have proved the most troublesome to manage. There is an overwhelming majority (86·5%) of good

TABLE 3
RESULTS OF TREATMENT OF LOW ANOMALIES

Type	Total	Deaths	Not Followed Up	No. Seen	Good	Fair	Poor	Average Follow-up (yrs)
Covered anus	53	3	8	42	37	5	—	3·1
Ectopic anus:								
Perineal and vulval	57	2	13	42	39	1	2	3·6
Vestibular	33	3	3	27	20	6	1	5·6
Vaginal	8			8	7	1		4·25
Stenosed anus	38	3	7	28	24	4		3·0
Anal membrane	3			3	3			2·4
	192	11	31	150	130	17	3	

TABLE 4
RESULTS: HIGH ABNORMALITIES

Type	Total	No. Seen	Good	Fair	Poor
Pull-through at birth	24	19	7	9	3
Colostomy at birth, pull-through later	29	29	7	14	8
Colostomy at birth, perineal dissection later	8	8	4	2	2
Perineal operations at birth and later	7	6	2	2	2
Colostomy at birth, sacral operation later	1	1	1		
	69	63	21	27	15

TABLE 5
MORTALITY RATES

Anomalies	No. of Cases	Deaths	
Low:			
Covered anus	53	3	5·7%
Ectopic anus	98	5	
Stenosed anus	38	3	
Anal membrane	—		
High:			
Anorectal agenesis	114	36*	35·9%
Rectal atresia	5	2	
Cloaca	9	5	
Multiple abnormalities	3	3	

* Corrected mortality anorectal agenesis alone is 46%. (See text).

results. Several of these 'good' cases have spent a long time in the fair category before bowel habit has been restored to normal, and this stresses the most important factor in treatment. These children *must* be watched carefully postoperatively. Dilatation of the new anus must be adequate but not excessive, or scarring and restenosis occurs. If constipation develops it must be treated energetically to avoid colonic inertia. Of the 20 'fair' or 'poor' results, 10 can be directly attributed to the anomaly not being recognized until the age of 6 months or later. The higher ectopic openings, i.e. the vaginal and vestibular are less stenosed at birth and so may remain unrecognized, presenting later with overflow incontinence or severe constipation. Another fact that emerges is that the stenosed anus (in our classification) in the normal site, tends not to restenose after adequate dilatation whereas the cutback anus often does.

High Anomalies. Rectal atresia has been treated by pulling the blind proximal bowel through the distal pouch; the treatment of cloaca has varied according to the anatomical abnormality, and there have been no survivors amongst the three cases of ectopia cloacae. The treatment of the cases of anorectal agenesis has been more difficult to analyse. 38 children were referred here having had a previous operation, the majority (27) with a simple colostomy (quite often this was an iliac colostomy which interfered with the later pull-through operation). All but two of these 38 required further operations and in 17 cases this was an abdomino-perineal and in 14 a perineal pull-through; two were pulled down by a sacral approach, two were eventually left with a permanent colostomy and one required only refashioning of the anus. In the neonatal period 76 children were seen and the two main forms of treatment were (1) immediate abdomino-perineal pull-through and division of fistula if present (33 cases), and (2) simple colostomy with or without division of a fistula (36 cases). This second routine was usually adopted in children in whom there were other abnormalities or who were unfit for a major operation. Of the total of 114 cases of anorectal agenesis 69 survivors have had operations providing an anus at the normal site; the results of these operations have been assessed in Table 4.

A result has been regarded as *good* when the child is continent of faeces and urine, has his bowels open spontaneously and regularly and appears to have some degree of rectal sensation in that a full lower bowel is recognized, and soiling is only an occasional accident. A *fair* result is one in which the child is continent of faeces except when these are unusually loose, although soiling may commonly occur, and in whom laxatives or suppositories are often required. A *poor* result signifies virtually a perineal colostomy.

There is, at first glance, little to choose between the results of the two principal forms of treatment. In the initial abdomino-perineal pull-through, however, there are still five children too young to assess. In the absence of other complications this is the operation which we now favour. If this is not possible we prefer initially to perform a colostomy and divide a fistula if present. The perineal and sacral operations have been abandoned.

There remain the mortality rates which are stated in Table 5. The overall mortality rate for the low anomalies is 5·7% and for the high 35·9%. Of rather more interest, however, is the mortality rate amongst the 76 cases of anorectal agenesis first seen and treated at this hospital (the remaining 38 of the total of 114 cases had been initially treated elsewhere). There were 35 deaths amongst these 76 infants, giving a mortality rate of 46%. This formidable figure is largely attributable to the high incidence of severe associated anomalies which were themselves the cause of death: no less than 24 of these 35 children were so affected.

Summary

The division of these anomalies into high and low types is of assistance both in treatment and prognosis, and is justified by the figures we have given and which bear repeating. Results of treatment show 86% good results in the low cases compared with 30% in the high; 25% of the low cases have associated anomalies, compared with 62% of the high, and the latter are usually of a more severe nature. The mortality rate for the low cases is 5·7% and for the high cases 35·9%, and this figure if corrected for anorectal agenesis seen and treated in the neonatal period rises to 46%.

This is the largest series of these cases yet recorded. Well-documented series have been reported from the United States, but unfortunately comparison with our results is impossible owing to differences of classification, e.g. the covered anus in our classification is a low anomaly, in Ladd's classification it would be Type 3 and be grouped with the high anomaly we call anorectal agenesis. There is certainly a place for standardization of nomenclature and we hope that this system will recommend itself.

We would like to thank the Surgeons of The Hospital for Sick Children, Great Ormond Street, for permission to report their cases. My own thanks I gratefully offer to Mr. H. H. Nixon, F.R.C.S. for helpful criticism and advice, and to Mr. Geoffrey Lythe for the illustrations and diagrams.

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High Anomalies. Rectal atresia has been treated by pulling the blind proximal bowel through the distal pouch; the treatment of cloaca has varied according to the anatomical abnormality, and there have been no survivors amongst the three cases of ectopia cloacae. The treatment of the cases of anorectal agenesis has been more difficult to analyse. 38 children were referred here having had a previous operation, the majority (27) with a simple colostomy (quite often this was an iliac colostomy which interfered with the later pull-through operation). All but two of these 38 required further operations and in 17 cases this was an abdomino-perineal and in 14 a perineal pull-through; two were pulled down by a sacral approach, two were eventually left with a permanent colostomy and one required only refashioning of the anus. In the neonatal period 76 children were seen and the two main forms of treatment were (1) immediate abdomino-perineal pull-through and division of fistula if present (33 cases), and (2) simple colostomy with or without division of a fistula (36 cases). This second routine was usually adopted in children in whom there were other abnormalities or who were unfit for a major operation. Of the total of 114 cases of anorectal agenesis 69 survivors have had operations providing an anus at the normal site; the results of these operations have been assessed in Table 4.

A result has been regarded as *good* when the child is continent of faeces and urine, has his bowels open spontaneously and regularly and appears to have some degree of rectal sensation in that a full lower bowel is recognized, and soiling is only an occasional accident. A *fair* result is one in which the child is continent of faeces except when these are unusually loose, although soiling may commonly occur, and in whom laxatives or suppositories are often required. A *poor* result signifies virtually a perineal colostomy.

There is, at first glance, little to choose between the results of the two principal forms of treatment. In the initial abdomino-perineal pull-through, however, there are still five children too young to assess. In the absence of other complications this is the operation which we now favour. If this is not possible we prefer initially to perform a colostomy and divide a fistula if present. The perineal and sacral operations have been abandoned.

There remain the mortality rates which are stated in Table 5. The overall mortality rate for the low anomalies is 5·7% and for the high 35·9%. Of rather more interest, however, is the mortality rate amongst the 76 cases of anorectal agenesis first seen and treated at this hospital (the remaining 38 of the total of 114 cases had been initially treated elsewhere). There were 35 deaths amongst these 76 infants, giving a mortality rate of 46%. This formidable figure is largely attributable to the high incidence of severe associated anomalies which were themselves the cause of death: no less than 24 of these 35 children were so affected.

Summary

The division of these anomalies into high and low types is of assistance both in treatment and prognosis, and is justified by the figures we have given and which bear repeating. Results of treatment show 86% good results in the low cases compared with 30% in the high; 25% of the low cases have associated anomalies, compared with 62% of the high, and the latter are usually of a more severe nature. The mortality rate for the low cases is 5·7% and for the high cases 35·9%, and this figure if corrected for anorectal agenesis seen and treated in the neonatal period rises to 46%.

This is the largest series of these cases yet recorded. Well-documented series have been reported from the United States, but unfortunately comparison with our results is impossible owing to differences of classification, e.g. the covered anus in our classification is a low anomaly, in Ladd's classification it would be Type 3 and be grouped with the high anomaly we call anorectal agenesis. There is certainly a place for standardization of nomenclature and we hope that this system will recommend itself.

We would like to thank the Surgeons of The Hospital for Sick Children, Great Ormond Street, for permission to report their cases. My own thanks I gratefully offer to Mr. H. H. Nixon, F.R.C.S. for helpful criticism and advice, and to Mr. Geoffrey Lythe for the illustrations and diagrams.

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FROM THE MERMAID TO ANAL IMPERFORATION: THE SYNDROME OF CAUDAL REGRESSION*

BY

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If the mermaid legend evokes more of mythology than of pathology, its origin very probably lies in ancient observations of certain types of human monstrosities.

Human sirens are not as rare as is sometimes thought; I have been able to examine two cases within the past year, and during that time I have been told of several others. I shall talk today of the usual findings and attempt to draw certain wider conclusions.

The fusion of the inferior limbs, the *symelia* (Fig. 1), which constitutes the characteristic element of the malformation to the observer, is not the only abnormality in these cases (Potter. 1952). The more constant findings in monsters of this general type may be summarized as follows (see Table 1):

1. Flexion and inversion in external rotation of the lower limbs.
2. Anomalies of the lumbar and sacral spine.
3. Imperforate anus.
4. Agenesis of the kidneys and urinary tract.
5. Agenesis of the internal genital organs, *with the exception of the gonads.*

The visceral anomalies are constant and uniform. It is these anomalies which are incompatible with life, while the symelia is the least grave and the more variable of the malformations presented by the siren. There are even sirenoid monsters in whom the lower limbs are flexed and turned into external rotation, but remain independent. These have been called the 'anchipod' type.

It is possible to produce the sirenoid monstrosity in chicken embryos by destruction of the axial portion of the caudal region, between the primitive origins of the pelvic anlage (Wolff, 1948).

If the injury is localized, the lower limbs are not fused, and the anchipodal anomaly is produced. Even more localized lesions may be produced, so that it is possible to spare the lower limbs, the Wolffian system, the vertebral column, and finally have malformations at the cloacal region only.

TABLE 1

CHARACTERISTIC ELEMENTS IN SIREN MONSTERS

Lower limb anomalies	Flexion, external rotation; union (symelia) and often atrophy
Vertebral anomalies	Increased in number (epistasis), *or* sacral agenesis
Anorectal agenesis	
Urinary tract anomalies	Bilateral renal agenesis; ureteral, vesical and urethral agenesis
Genital anomalies	Wollffian or Mullerian duct agenesis (gonads present in all cases)

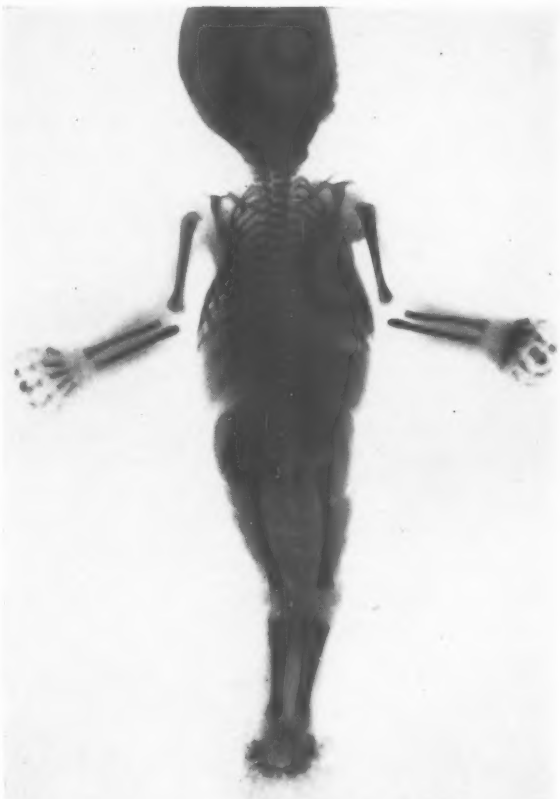
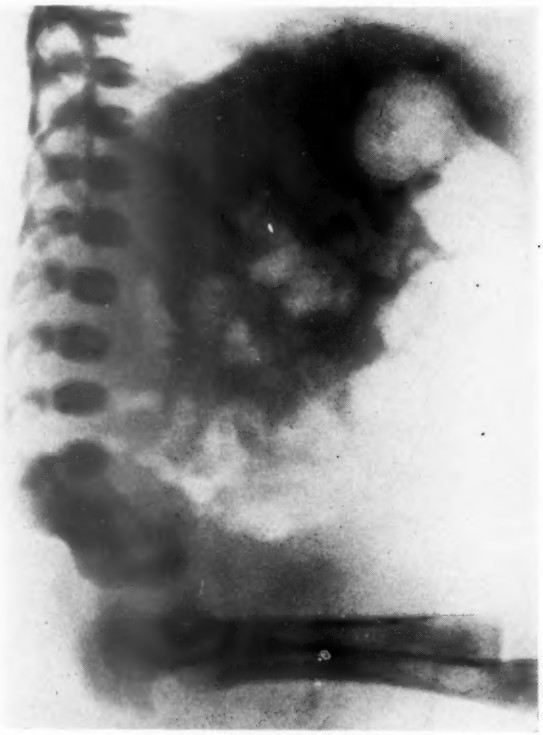


FIG. 1.—A human siren.

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

(a)



(b)

FIG. 2.—Sacral agenesis: (a) frontal and (b) lateral view.

These experimental findings infer that the siren
n onstrosity and malformations of the anal region
n ay perhaps represent the two extremes of one
c mprehensive syndrome, that of an embryonal
d fect in the formation of the caudal region. I have called this the 'syndrome of caudal regression', and I have attempted to verify its implications in human developmental pathology.

It is well known that anorectal malformations are rarely isolated (Prochiantz, 1957; Parkkulainen, 1957). According to several statistical studies, they are associated with other anomalies in 22 to 72% of cases. The latter figure is given by Moore and Lawrence (1952), who found, in careful necropsy studies of babies dying with anorectal anomalies, that 33 of 34 cases had other associated anomalies.

Unless one searches carefully and systematically for these anomalies, they may remain unnoticed. Often, however, they play an important part in the gravity of the total disorder, for functional disturbances resulting from these associated malformations may in themselves lead to death.

In 125 cases of anorectal malformations of Ladd types III and IV, there were 76 in which one or more other anomalies were present, an incidence of approximately 60% (Table 2). Since, in the early period, not all of these were studied systematically by radiography and other means, this is probably a minimal figure, and more recent studies have shown an increased proportion.

The most common anomalies in association with anal atresia are those of the vertebral column. I have found them to be present in 50 of the 125 cases. Williams and Nixon (1957) have also commented on their frequency. Included in these abnormalities are sacral agenesis (Fig. 2), vertebral dysmorphia (Figs. 3 and 4), hemivertebra and epistasis (Figs. 5 and 6). These may be found singly, or more often in association with one another (Duhamel, 1959; 1960).

Twenty-four infants were found to have an abnormality of the urinary tract. Of these, the most common was unilateral renal agenesis (Fig. 6). Seventeen showed genital anomalies, amongst which a uterine anomaly was very common (Fig. 7).

Finally, 13 of the cases presented malformation of the inferior limbs. These varied in degree to a considerable extent, and included club foot,

TABLE 2

125 CASES OF ANORECTAL MALFORMATIONS (LADD TYPES 3 AND 4)

Associated Congenital Anomalies in 76 Cases (60·8%)

Anomalies	No.	%
Vertebral	50	40
Urinary tract	24	19·2
Genital	17	13·6
Lower limb	13	10·4
Others	32	25·6

FIG. 3.

FIG. 3 —Vertebral dysmorphia.

FIG. 4.

FIG. 4.—Sacral dysmorphia.

FIG. 5.—Epistasis
A. 12th ribs.
B. Lumbosacral angle.
C. Coccyx.

FIG. 6.—Epistasis, right renal agenesis, left renal malformation.

FIG. 5.

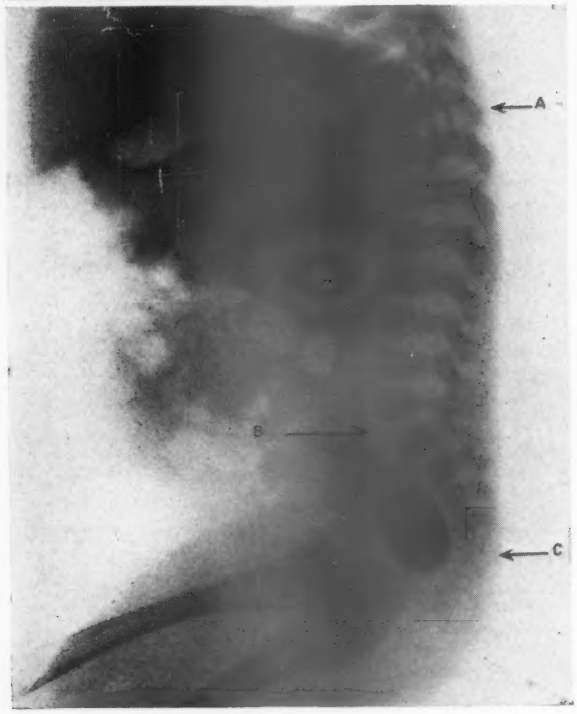


FIG. 6.

FIG. 7.—Uterine anomaly.

FIG. 8.—A human anchipodal monster.

atrophy of the limbs, defective motion of the joints, and in one case flexion and external rotation of the limbs exactly comparable with that found in the anchipodal monster (Fig. 8).

Other anomalies which were found in 32 infants, 21 of whom also had one or more of the malformations listed above, included congenital heart disease, abnormalities of the thumb, and mongolism.

The most frequent malformations associated with anorectal anomalies, therefore, are just those which one finds constantly in the siren, and which can be produced experimentally in the chick embryo by injury to its caudal pole.

In 65 of my 125 cases such malformations were found to be present. In 30 the findings were such that a true *syndrome of caudal regression* could be considered to exist. Three of the elements listed in the siren monstrosity were present in 17 cases, four were present in 11 and in two all five were found.

The 'syndrome of caudal regression', therefore, shows in variable proportion anomalies of the rectum, of the urinary and genital systems, of the lumbosacral spine, and of the lower limbs.

I have attempted to define this syndrome by means of comprehensive study of infants with anorectal abnormalities. I believe that similar studies by urologists, gynaecologists, and orthopaedic surgeons, carried out systematically in all cases of this type of anomaly, will show a similarly high percentage of malformations associated in this syndrome.

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IMPERFORATE VAGINA IN THE NEWBORN*

NEONATAL HYDROCOLPOS

BY

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The purpose of the present communication is to discuss hydrocolpos and hydrometrocolpos, a not uncommon complication of imperforate vagina in the newborn. We do not propose to discuss the relatively common problem of vaginal occlusion due to labial adhesions (Fig. 1), which can be easily separated with little or no bleeding.

Hydrocolpos in the newborn female due to imperforate hymen or to occlusion by a membrane in the lower third of the vagina is not excessively rare. At or shortly after birth the infant presents with lower abdominal swelling and a bulging membrane is seen at the vaginal orifice (Fig. 2). This bulging membrane looks like a cystocele and when gently reduced the urethral orifice can be seen anteriorly. Occasionally there may be a tiny opening in the occluding membrane through which a white mucoid material can be extruded. The anomaly has been fully described by Mahoney and Chamberlain (1940), by Gross (1953), by Caffey (1956), and by many others and for the purposes of the present communication a brief description of their findings will be sufficient.

In this condition the vagina is invariably greatly distended—*hydrocolpos*—and on occasions the accumulated fluid can stretch the cervical canal and the body of the uterus as well—*hydrometrocolpos*—though we have seen the uterine cavity distended only on one occasion. The ballooned genital tract arises from the pelvic floor into the abdominal cavity. The cyst is filled with clear or mucoid fluid which tends to become purulent from bacterial invasion, giving rise to *pyocolpos*. The uterine tubes have not been involved in any of the reported cases. The distended genital tract may cause urinary obstruction and the enlargement of the bladder may hinder palpation of the vaginal cyst. Megaloureter and hydronephrosis may follow and pyuria will be a further complication. Posterior pressure may cause rectal obstruction. There may be respiratory embarrassment through the upward displacement of the abdominal contents. On digital rectal examination the pelvis is filled by a mass projecting against the hollow of the sacrum. On inspection of the vagina a bulging membrane is seen at or above the hymen. In such patients a needle is inserted through the membrane and fluid is aspirated to confirm the diagnosis. Radio-opaque fluid may be instilled to outline the obstructed vagina (Fig. 3). Having made the diagnosis the occluding membrane is slit with a knife and the cyst contents are evacuated.

Less commonly the hydrocolpos is due to atresia of the lower vagina (White and Dennison, 1958) and

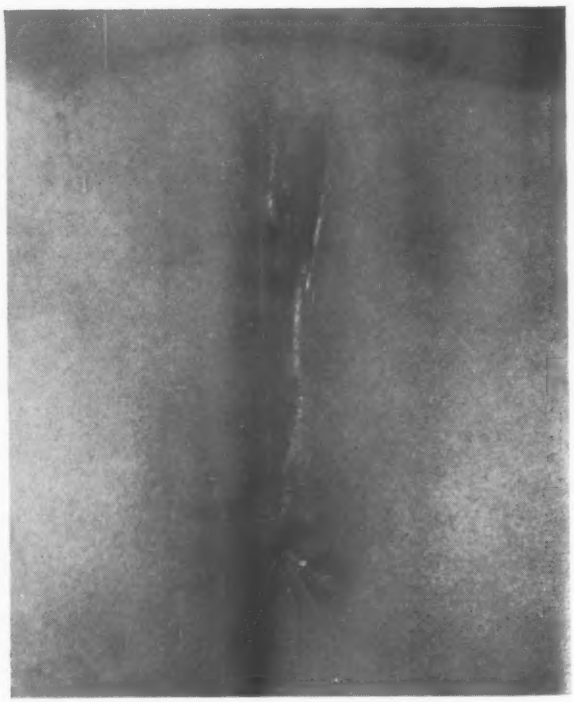

FIG. 1.—Occlusion of vagina due to labial adhesions.

FIG. 2.-

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

FIG. 2.—Hydrocolpos, showing bulging membrane at the vaginal orifice.

FIG. 3.—Vaginogram in infant with hydrocolpos.

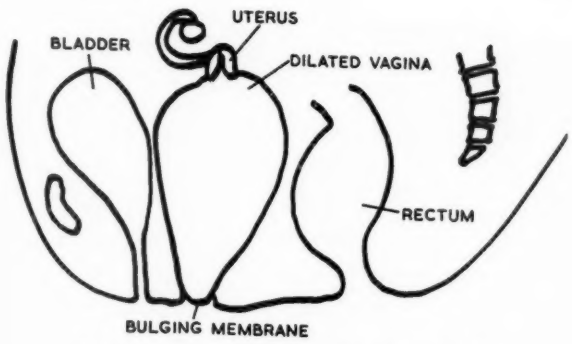

FIG. 4.—Hydrocolpos due to membrane occlusion.

in our limited experience of five cases the diagnosis was finally confirmed only at laparotomy. One of us (W.M.D.) first encountered this condition some 10 years ago and the account of his misdemeanours may serve as an awful warning to any junior colleague. A very ill baby, 1 day old, was admitted suffering from peritonitis and intestinal obstruction. At laparotomy dense adhesions were found and a large supravaginal (? urachal) cyst was demonstrated. This was freed, the ureters dissected off and the cyst excised *in toto*. When the specimen was examined later, it became evident that the operator had performed what is probably the earliest panhysterectomy on record! The so-called urachal cyst consisted of a grossly distended vagina on top of which was a tiny uterus complete with tubes and ovaries. The patient did not survive surgical intervention.

Figs. 4 and 5 show in a schematic fashion the essential anatomical differences between vaginal occlusion by a membrane, a simple well-known problem and the relatively undocumented hydrocolpos due to vaginal atresia. In spite of the anatomical differences the clinical features and the

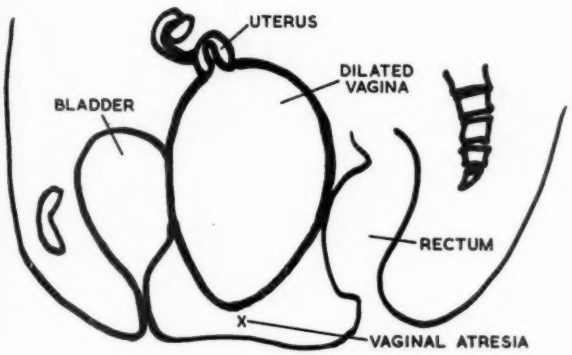

FIG. 5.—Hydrocolpos associated with vaginal atresia.

complications are similar when the hydrocolpos is due to atresia of the vagina. During the past few years we have been particularly unlucky to encounter five infants with atresia of the lower vagina. In all these cases there was a solid block of tissues (at least 2 cm.) separating the distended vagina from the perineum and there was no bulging membrane present to aid diagnosis. In spite of this we have confidently diagnosed hydrocolpos due to vaginal atresia in all these infants, four babies and one girl aged 7 months. Unfortunately only one of our five patients is alive and well and she has lost both her vagina and her uterus.

In the newborn babies dense adhesions make exploration of the abdomen difficult. The cysts vary from 10 to 15 cm. in diameter and in two of the four babies the 'cyst' contents were grossly infected (pyocolpos). In only one case was the uterus distended (hydrometrocolpos). On three occasions the cyst was evacuated through the abdomen and no attempt was made to drain the vagina via the perineum. In the uninfected case it was theoretically possible to evacuate the cyst through the abdomen and after dissecting down towards the lower pole of the cyst to pass a probe through the inferior pole of the cyst until it presented behind the urethra in the region of the posterior fornix. A perineal incision over the probe allows drainage of the distended vagina through an indwelling Malecot catheter. It was difficult to visualize the next stage, as it was assumed that the resulting fibrosis following repeated dilatation would make a later McIndoe and Banister (1938) operation almost impossible. In anticipation it was thought that it might be possible to maintain the passage by using a split-skin graft over a mould until the patient was old enough for construction of an artificial vagina. Having learned from our bitter experience, Mr. John Grant, of our Staff, recently dealt with a non-infected hydrocolpos in an older infant. Before evacuating the cyst he carefully dissected down into the pelvis only to find that suddenly an intact cyst was delivered into the abdomen (Fig. 6). The only reasonable solution to the problem then was to separate the tubes and the ovaries, to remove the vaginal cyst and the uterus and to leave the ovaries behind. This infant made an uneventful recovery and remains well.

From the aforesaid it will be evident that we in Glasgow, as yet, do not know how to deal successfully with hydrocolpos or hydrometrocolpos due to vaginal atresia. On the other hand, to the best of our knowledge, there is no evidence of any more encouraging results from other centres.

One could therefore legitimately ask: Why is the anomaly so rare? Haematocolpos at or shortly after puberty is well known. Due to an imperforate hymen the uterine discharge collects within the vagina and the girl presents with abdominal or pelvic pain. There is tenderness on suprapubic pressure and the ballooned vagina can be felt on rectal examination. This condition should be suspected in a girl with pubic hair and enlargement of the breasts who has not yet menstruated. Why do these girls not present with hydrocolpos in the neonatal period? Obstruction of the vagina alone does not normally give rise to symptoms until puberty. One must therefore postulate that apart from the vaginal obstruction, which provides the necessary anatomical conditions, the real cause lies in the over-abundant secretory activity of the neonatal uterine or cervical glands.

FIG. 6.—Intact vaginal 'cyst' and uterus.

In order to find some support in favour of this postulate we have been reinvestigating during the past four years certain aspects of the development of the vagina and also some features of the physiology of the neonatal reproductive organs. Our findings and conclusions, together with the discussion of the relevant literature, will be presented elsewhere and for the time being we shall confine ourselves to the following brief statements.

Contrary to the most generally accepted view in

the Anglo-American textbooks, according to which only the lower fifth of the vagina is formed by the fused 'sino-vaginal bulbs' growing out from the dorsal wall of the urogenital sinus, we believe with Villas (1932), Politzer (1955) and Bulmer (1957) that the boundary between the sinus and Mullerian derivatives of the human vagina lies either near to the portio vaginalis or in the cervical canal. We can also confirm Politzer's (1955) observations on the surprisingly great variability of the grade of development of the vagina in foetuses of similar ages and we believe that sometimes the neonatal vagina and uterus can be too immature histologically to be able to respond to hormonal stimuli in the normal fashion.

It is accepted that in general the uterus of the newborn shows a considerable degree of precocious maturity and there is a marked hyperplasia of the lining epithelium and of the glands (Rosenthal and Hellman, 1952). In fact these glands produce a copious mucus secretion, presumably, under the impact of oestrogens and progesterone derived both from the placenta (Brown, 1959) and from the foetal ovaries (Ober and Bernstein, 1955). While there is a tacit assumption that this mucus secretion is largely the product of the glands of the body of the uterus, our own observations revealed a surprisingly greater maturity of the glands of the cervical canal and we believe that these glands are the main, if not the exclusive source of the mucus discharge. With regard to the hormonal control of the secretion of the cervical glands of the uterus there is accumulating evidence to indicate the cardinal role played by oestrogens (Moricard, 1936; Watson, 1939). Later it is shown (Aberbanel, 1946; Zondek and Rozin, 1954; Macdonald and Sharman, 1959; Stern, 1960) that administration of progesterone inhibits cervical mucus secretion.

Most authorities remark on the great individual variations that exist in the urinary output of oestrogens during pregnancy and we believe that the non-appearance of hydrocolpos in some cases of imperforate vagina of the newborn may be due to the low output of oestrogens or in some instances to the blocking effect of increased discharge of progesterone or progesterone-like substances from the placenta or more likely from the foetal adrenal cortex.

While the above two hypotheses could account for the dormancy in an odd case of imperforate vagina, it would stretch the imagination too far to expect them to account for the large number of cases observed in the adult by Bryan, Nigro and Counseller (1949), by McIndoe (1959) and by Simmons (1959). Clearly we must look for some other explanation. In this respect it seems to us highly significant that in the majority of the adult cases of congenital absence of the vagina or of vaginal atresia, palpation or laparotomy reveals ovarian agenesis or some other malformation of the internal reproductive organs. Thus, while in the cases occurring among newborn babies and small infants the abnormality is strictly and exclusively confined to the vagina, a derivative of the urogenital sinus, in the adult cases both urogenital sinus and Mullerian structures are involved and create an anatomical situation with entirely different physiological behaviour and clinical manifestations. Consequently we believe that the two groups should be treated as separate clinical entities which can be usefully compared but should not be confused with each other.

Our main objective in putting forward these somewhat provocative ideas is two-fold: partly we seek advice from our learned audience concerning the acceptability of these views and partly we hope that by reaching some agreement we may gain a closer understanding of the aetiology and also obtain a necessary theoretical basis for the correct treatment of neonatal hydrocolpos and hydrometrocolpos due to vaginal atresia.

We thank Mr. J. R. Devlin for preparing the illustrations and Dr. A. M. MacDonald, Dr. S. P. Rawson and Mr. John Grant for their co-operation in our investigations.

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GASTRIC ATRESIA*

BY

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In the newborn a complete occlusion of the pyloric outlet of the stomach is an extremely rare event. Very early vomiting occurs due to an absolute stoppage, but the vomitus contains no bile as found in stenosis or atresia below the ampulla of Vater. Respiratory troubles occur very quickly from breathing the overflowing stomach contents. The cause of stomach obstruction may be different. Pyloric spasm in the newborn is rare. Cystic masses in the gastric wall have been described.

Case Report

This case reports an intrinsic occlusion due to a membrane. The premature female infant, weighing 2,500 g., vomited mucus fluid on the second day after birth and later vomited her feeds; there was no bile, but meconium was passed. On admission at the age of 6 days her weight was 1,900 g. A flat plane radiograph of the abdomen showed gas in the stomach, but none in the duodenum or the remainder of the small bowel (Fig. 1).

Despite the fact that the absence of gas in the rest of the abdomen is also typical of an atresia, operation was performed on the supposition of a pyloric spasm. We even found a very slight hypertrophy of the pyloric bulge and slit it following Weber-Ramstedt. But postoperatively the child continued vomiting and another radiograph showed there was no gas in the bowel. Three days later a further laparotomy had to be performed. The stomach was opened from a gastrotomy in the antral area. It was impossible to probe the pyloric channel because of a complete obstruction due to a solid membrane between antrum and pyloric channel (Fig. 2). After perforating the membrane and dilating the opening, a tube was inserted into the duodenum (Fig. 3). The passage was then free, the child could be fed through the tube and bowel movements were satisfactory. A further radiograph taken two weeks after the operation showed the opaque medium passing the pylorus beside the tube.

A short time later the child began vomiting again and the fluid residues in the stomach increased. It was decided at this third operation to perform a gastrojejunostomy. Postoperatively the passage through the anastomosis slowly began to work (Fig. 4). Nevertheless, the course was a dramatic one because of disturbances of electrolytic balance as well as troubles from respiratory and circulatory systems. For a long time the child did not gain weight and only recently has there been a constant increase in weight.

Discussion

In the literature we have found only 10 cases of children operated upon in the first 12 days of life for a complete gastric occlusion. Bennett (1937), Touroff and Sussman (1940), and Fell (1951) found, as we did, the cause in a prepyloric diaphragm. Burnett and Halpert (1947) and Brown and Hertzler (1959) in other cases observed connective tissue up to 1 cm. in length in the pyloric area, completely occluding the pyloric channel. A very interesting paper was given by Metz, Householder and DePree (1941). They found two membranes at a distance of 6 cm. with a tumour palpable through the abdominal wall, containing gastric juice. From the 10 cases dealt with, five had been operated on successfully and re-examination showed free passage and a normal gastric function.

The cause of gastric atresia is almost unknown. In the foetal stage the stomach is at first a hollow organ. Until now no solid stage has been found, as is observed with the rest of the bowel in the fifth to tenth week of foetal life. Therefore an insufficient recanalization of solid stage as supposed in duodenal atresia cannot be the cause of gastric atresia. Touroff and Sussman believe that a fusion of the mucous membrane folds during the development of the pyloric bulges leads to the diaphragmatic occlusion.

In complete gastric obstruction indication for operation is clear. Pyloric spasm in the newborn rarely indicates complete absence of gas in the bowel; generally speaking, absence of gas in the bowel and vomitus without bile indicate a complete occlusion above the ampulla of Vater, either a membrane or atresia. Confusion with pyloric spasm is sometimes made and is described for instance by Bennett (1937).

The question remains as to what to do in atresia of the pyloric outlet of the stomach. An operative excision of a membrane by gastrotomy leads to

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

FIG. 1.

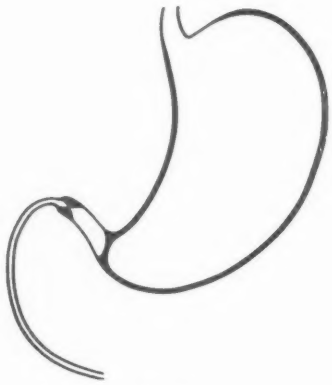

FIG. 2.

FIG. 1.—Antero-posterior radiograph, showing gaseous distension limited to the stomach.

FIG. 2.—Diagram of the stomach with the intrinsic obstruction.

FIG. 3.—After opening the stomach in the antral area and perforating the membrane a tube was inserted into the duodenum.

FIG. 4.—Radiograph taken two weeks after performing the gastro-enterostomy, showing satisfactory passage of the opaque medium into the small bowel.

FIG. 4.

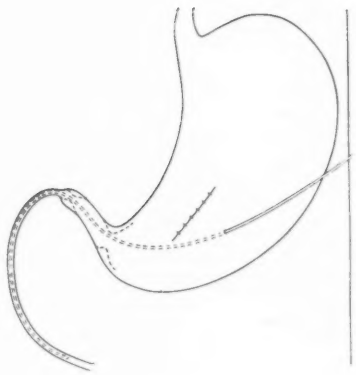

FIG. 3.

technical difficulties due to the considerable hypoplasia of the duodenum beyond the membrane. During excision damage to the wall may occur. To prevent this one can fill up the duodenum with sodium solution, so that the membrane will bulge slightly into the stomach. It is possible now to resect the central part and slit the border radially. Brown and Hertzler (1959) reported on two children with connective tissue 0·6 cm. in length in the pyloric channel, found by a longitudinal incision of the pylorus. They opened the blind-ending sacks of mucous membrane and performed an anastomosis over a tube and finally closed the incision laterally.

We found quite different features in another case with a very small opening in the membrane. A 5-week-old child presented with a postpyloric membrane and we performed the excision without difficulty by gastrotomy. Unlike the child with complete occlusion, a great deal of air and fluid had run through the small opening; the duodenum and the distal bowel were functioning and therefore were of nearly normal calibre. This enlargement of calibre beyond the membrane considerably facilitates the excision and makes it fairly safe.

The perforation we tried seems questionable and cannot be more than a temporary help. Nevertheless, the perforation worked as a congenital opening, and led to improved bowel function facilitating the gastroenterostomy. There will not always be such good results as in the case of Benson and Coury (1951), who performed a gastroenterostomy after perforation and later found a free pyloric passage with closed anastomosis.

Because of the well-known disadvantages and dangers of a gastrojejunostomy, the decision to perform one is taken reluctantly. Three of the 10 children with gastroenterostomy died a few days after operation. One of these had a suture leakage and pneumonia and two others suffered from ileus, the exact cause for which was not known (Holladay 1946; Salzberg and Collins, 1960).

Possibly the complicated conditions of a gastrojejunostomy have been the cause of our child not progressing over a month. Until now there have been few reports of gastroenterostomy in the newborn, but the poor results in adults seem to prohibit its use in the newborn. What remains is pylorus resection or gastroduodenostomy, neither of which are particularly successful in the newborn infant. It is another question, whether we should use it in our case as a secondary step with removal of the gastroenterostomy after enlargement of the duodenum and small bowel and recovery by the child. In this way it would perhaps be possible to achieve somewhat normal conditions. On the other hand, such an intervention would not be simple or without risk in view of the fact that the child's abdomen has already been operated on three times.

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AUTOTRANSPLANTATION IN LINGUAL ECTOPIA OF THE THYROID GLAND*

REVIEW OF THE LITERATURE AND REPORT OF A SUCCESSFUL CASE

BY

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Though 'lingual thyroid' has been an accepted term for many years, precise terminology might be served better by the use of ectopia to indicate those cases—the majority—in which no thyroid tissue exists in the orthotopic (prelaryngeal) site, the prefix lingual indicating the site of ectopia. Ectopia also serves to describe the situation in which a 'thyroglossal cyst' is solid and represents the only thyroid tissue which the patient possesses. Such cases are analogous to lingual ectopia, the difference lying in the point at which migration is arrested. If this designation is accepted, the term 'aberrant thyroid' could be reserved for those cases in which orthotopic thyroid tissue coexists.

The introduction of radioactive iodine I^{131} uptake surveys has made it possible to determine the exact site or sites of functioning thyroid tissue, and has displaced both biopsy of ectopic lingual tissue and cervical exploration for orthotopic thyroid.

Since Hickman (1869) described the first case, experience of lingual ectopia of the thyroid gland has steadily accumulated and there are now over 200 cases on record. Montgomery (1936) in a critical review suggested criteria for authenticity and at that time accepted 144 cases as proven. His criteria were:

1. A lingual tumour situated between the epiglottis and the circumvallate papillae.
2. Biopsy of the tumour demonstrating the presence of thyroid tissue.
3. As an alternative, the supervention of a hypothyroid state on operative removal of the tumour.

Clinical signs or symptoms have appeared during puberty or adolescence in almost half of the cases recorded. They can be summarized as follows:

1. The most common symptoms were those of oropharyngeal obstruction, e.g. dysphagia, dysarthria, dyspnoea, orthopnoea.
2. Haemorrhage, often recurrent and in small amounts, occurred from dilated submucous venules on the surface of the lingual mass.
3. Disturbances of thyroid function.

Montgomery's series contained four cases showing features of hyperthyroidism and 21 of hypothyroidism.

Oral examination reveals a pink, grey or red swelling looming over the horizon of the tongue, which is best seen with the aid of traction and depression of the tongue.

In contemporary practice radioactive iodine I^{131} 'uptake' survey is the most valuable investigatory procedure, for it confirms or disproves the diagnosis and indicates the presence or absence of orthotopic thyroid tissue.

Case Report

A 9-year-old girl was referred for consultation in June, 1958, because of a tumour and respiratory obstruction noted during anaesthesia and tonsillectomy; this had been undertaken for snoring and mouth breathing. Her mother had noticed a change in the girl's voice, huskiness and dysarthria becoming more marked over a period of two years. Recently mild dysphagia had appeared and noisy mouth breathing was present during sleep. The patient had lived in Traralgon all her life, an area of Victoria recognized as goitrogenic. Iodized domestic salt had been used in the household, this being the common practice in the region. Her health in the past had been good and there was no other relevant history.

General examination showed a solidly-built and normally developed prepubertal girl, the only apparent physical abnormality being a reddish spherical tumour projecting above the dorsum of the tongue in the region of the foramen caecum. There was a peculiar empty feeling between the sternomastoid muscles and the thyroid cartilage.

Investigation. On July 7, 1958, a tracer dose of 5·8 μc. of I^{131} was administered orally, and followed 24 hours later by scintillometry which showed that I^{131} was concentrated in the region of the base of the tongue approximately 8 cm. above the sternal notch. There was no

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

significant uptake in the normal thyroid region. The 24-hour retention of I^{131} in the lingual area was 60% of the oral dose. Surgical treatment was decided upon. Oral tetracycline (250 mg.) and penicillin (250 mg.) were administered at six-hour intervals commencing two days before operation on July 16. Premedication of inj. papaveritum (10 mg.) with L-hyoscine hydrobromide (0·2 mg.) was given 45 minutes before anaesthesia which was induced with intravenous thiopentone (200 mg.) augmented with nitrous oxide, oxygen and halothane mixture. Two injections of 'scoline', succinylcholine chloride (50 mg.) were necessary to achieve per-nasal intubation of the larynx, performed 'blind' by fingertip touch guidance. The tumour prevented the introduction of a laryngoscope. Anaesthesia was then continued with 1·3% halothane in nitrous oxide and oxygen mixture.

Operation. When the tongue was forcefully drawn forwards with several chromic sutures, the swelling was still inaccessible. Right lateral pharyngotomy was chosen as the alternative route, as the tumour extended more towards this side (Fig. 1). A slightly curved incision was made over the submandibular area (Fig. 2); the platysma and fascia were divided in the line of the incision and reflected upwards with the unidentified cervical branch of the facial nerve. The anterior facial vein and facial artery were divided and the submandibular gland excised, the deep portion of the gland being withdrawn from beneath mylohyoid muscle, and the submandibular duct severed after identifying the lingual nerve (Fig. 3).

The intermediate tendon of the digastric muscle was then divided, and the posterior belly turned laterally to display the greatly enlarged and tortuous lingual artery (Fig. 4).

By dividing the hyoglossus muscle, with its nerve supply, and retracting both lingual and hypoglossal nerves cranially, the pharyngeal wall and middle constrictor of the pharynx were displayed (Fig. 5).

The pharynx was opened by an oblique curved incision giving the exposure indicated in Fig. 6 which has been interpreted with some licence to permit orientation.

Pressure exerted by an assistant's finger in the mouth dislocated the mass into the incision (Fig. 7). As no plane of cleavage existed between tumour and tongue, scissor dissection and suture ligatures were necessary to free the inferior and anterior aspects.

Haemostasis and closure of the depression in the tongue were effected by atraumatic chromic sutures. The front of the epiglottis had been denuded of mucous membrane and the possibility of postoperative oedema in the area was considered sufficient indication for tracheostomy.

Reconstitution of each stratum was performed, and a small roll of dental dam drain led from the closed pharyngeal wall incision to the exterior through a small separate stab.

Transplantation was commenced during closure of the cervical incision. The excised mass was denuded of mucous membrane, cut into slices and then 2-3 mm. cubes. A transverse lower abdominal incision was made and the anterior rectus sheath opened vertically. Tone in the rectus muscle fibres at first ejected the cubes of tissue until a further 50 mg. of succinylcholine chloride were administered. The relaxed rectus fibres were parted and groups of 5-6 cubes were inserted at several points, totalling approximately 150 $mm.^3$ of thyroid tissue. A fine catgut suture was placed across each group of parted muscle fibres to retain the cubes in position.

Tracheostomy was then performed, the cannula insertion being synchronous with anaesthetic extubation.

Microscopy. Sections of the ectopic thyroid gland showed a preponderance of foetal adenoma pattern, with a few scattered areas of colloid formation (Fig. 8). The macroscopic specimen had been hastily sliced for transplantation and there was inadequate material for a complete examination of the base of the tumour and its relation to the underlying muscle of the tongue.

Postoperative Course. The postoperative course was uneventful apart from muscular weakness of the right angle of the mouth which recovered in six weeks. The tracheostomy in retrospect was found to have been unnecessary, and the cannula was removed on the fifth postoperative day. All sutures were removed by the seventh day, and chemotherapy was discontinued at this time. Twelve days after operation a basal metabolic rate (B.M.R.) estimation was −24 and the serum cholesterol level was 380 mg. per 100 ml. This coincided with a temporary clinical picture of a mild hypothyroid state. She gained weight and appeared quiet and lethargic. This may have been in part a reaction to her experiences in hospital.

Scintillometry was repeated five weeks after operation and showed that a very small amount of I^{131} (some 4-5% of the oral dose) was concentrated in the lingual region. This count was obtained in the midline 8 cm. above the sternal notch. In the region of the autograft there was an uptake of the order of 20% of the total dose of 10 μc. A B.M.R. estimation at this time was −8 and a reading one month later was +8. This corresponded with a definite improvement in the patient's general appearance and suggested probable return to a euthyroid state. There was thus strong evidence that the autografted tissue was functioning within five weeks of operation and after a period of mild hypothyroidism. No thyroid substitutes were administered at any time.

She was reviewed at the age of 11 years in April 1960, when the tongue was normal. Puberty was well advanced and though no menarche had occurred, breast and pubic hair development were virtually adult in degree. A B.M.R estimation was +1; serum cholesterol, 312 mg. %; serum alkaline phosphatase, 23 Wohlgemuth units; her radiographic epiphyseal age was normal. Electrocardiography showed low voltage complexes possibly compatible with mild hypothyroidism.

An estimation of protein-bound iodine (P.B.I.) was 4·8 μg. (normal range 3·0-7·5 mg. %). A course of thyroid stimulating hormone (T.S.H.) was then administered as Organon Laboratory 'Ambinon B', an unstandardized mixture of T.S.H. and gonadotropins. Four

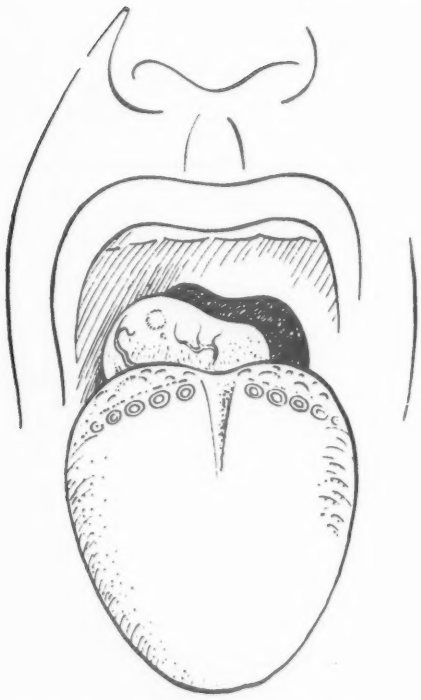

FIG. 1.—The lesion in the mouth with full traction on the tongue

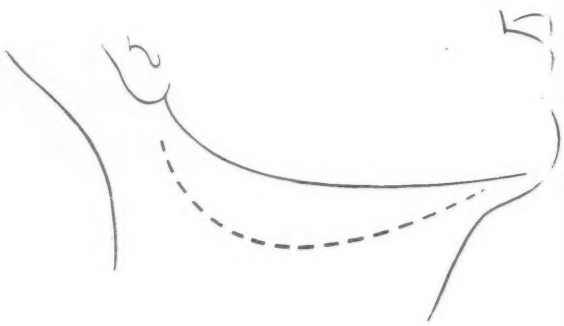

FIG. 2.—The incision.

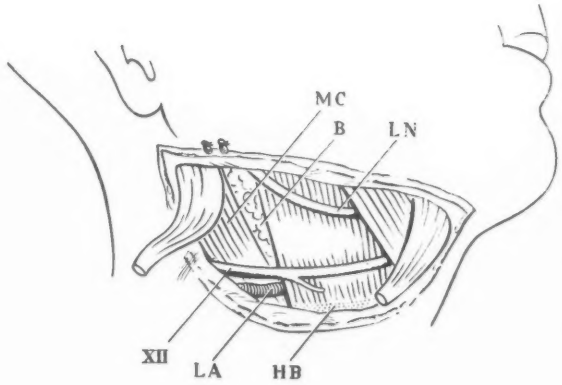

FIG. 4.—The floor of the digastric triangle.

MC: Middle constrictor muscle.
B: Buccopharyngeal fascia.
LN: Lingual nerve.
XII: Hypoglossal nerve and branch to hyoglossus muscle.
LA: Lingual artery.
HB: Greater cornu of hyoid bone.

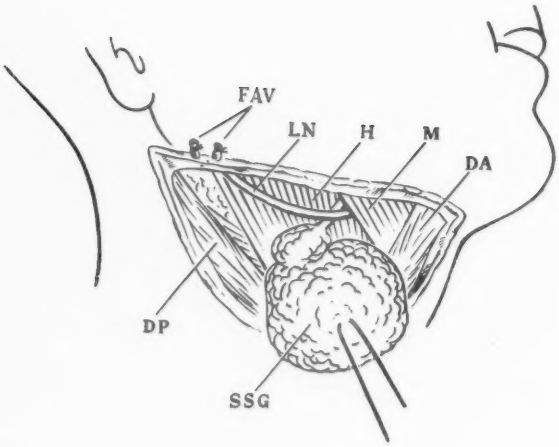

FIG. 3.—The removal of the submandibular gland.

FAV: Facial artery and vein.
LN: Lingual nerve.
H: Hypoglossus muscle.
M: Mylohyoid muscle.
DA: Digastric anterior belly.
DP: Digastric posterior belly.
SSG: Submandibular gland.

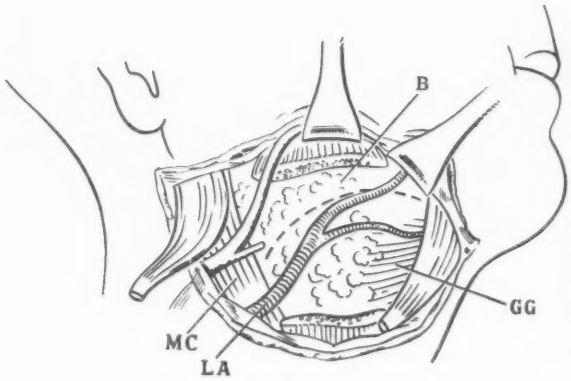

FIG. 5.—The greatly enlarged lingual artery and wall of pharynx after division of the hyoglossus muscle.
GG: Genioglossus muscle fibres.

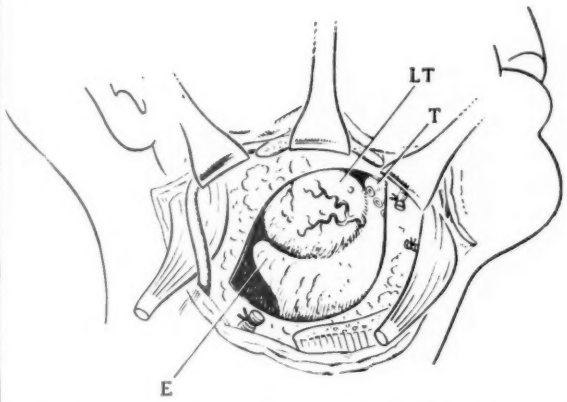

FIG. 6.—The pharynx opened to show the access to area of lingual ectopia.
LT: Lingual thyroid.
T: Tongue (circumvallate papillae).
E: Epiglottis.

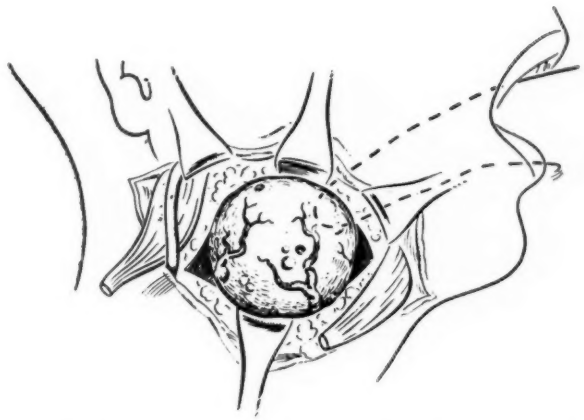

FIG. 7.—The lingual mass displaced into the incision by a finger inserted into the mouth.

injections of 1 ml. were administered intramuscularly at 12-hour intervals and a second P.B.I. estimation of 5·8 μg. % was then obtained. The potency of this preparation was confirmed by a biological assay. The assessment of her thyroid function, based on the first P.B.I. value, was considered to be within normal limits.

The response to T.S.H. showed a low thyroid reserve which must be interpreted in the context of peak pubertal demands. The '48-hour response', a measure of thyroid hormone stored in the gland, was low, which might be expected when estimated during the physiological 'stress' which puberty entails.

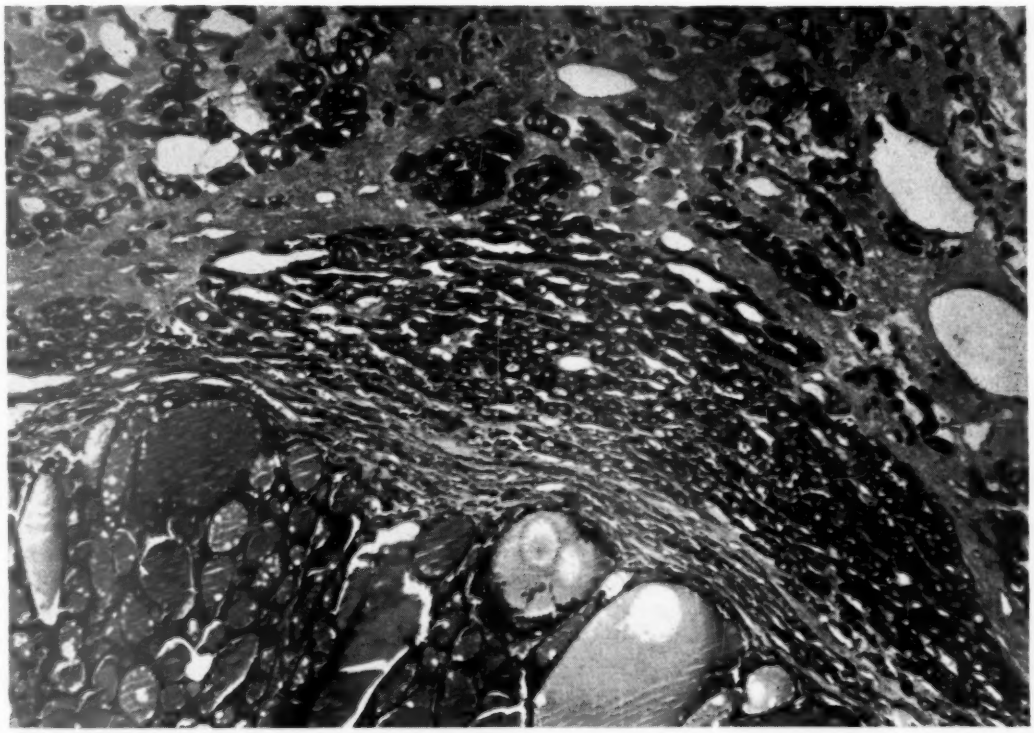

FIG. [illegible]—Section of the ectopic thyroid mass, showing 'foetal adenoma' pattern which predominated, and an area of colloid vesicle formation below.

Discussion

Embryology. Descriptions of thyroid development differ slightly concerning the median and lateral components. All concur that the median thyroid diverticulum developing from the floor of the embryonic pharynx is a bilobed flask-like structure at the 5-mm. stage. Shortly after the 10-mm. stage each lobe becomes contiguous on its outer side with the ventral components from each fourth pharyngeal pouch. The intimate relationship is accepted, but opinions differ as to how much if any, of the mature thyroid is contributed by the fourth arch (Hamilton, Boyd and Mossman, 1952).

This undetermined factor might account for the coexistence of ectopic thyroid tissue and orthotopic tissue in an individual patient. The situation was more obscure before I^{131} studies were available. Montgomery (1936) concluded that 70% of cases of lingual ectopia had no orthotopic thyroid. More recently Ward, Cantrell and Allan (1954) reported that of eight cases of lingual ectopia investigated with I^{131}, seven showed no orthotopic thyroid present, and the eighth case was probably identical, but documentation was incomplete. It must therefore be assumed that the lingual ectopic thyroid represents the only functioning tissue until I^{131} survey confirms this assumption or, an unlikely event, disproves it.

Indications for Operation. Occasionally lingual ectopia is discovered at necropsy without a history of symptoms and there may well be in the community individuals with asymptomatic thyroid ectopia who never seek treatment. Those with symptoms demand relief and it is they in whom the diagnosis is made and for whom treatment is required. Even if a lingual thyroid mass were an incidental clinical finding, treatment might be necessary to prevent the development of obstructive symptoms and haemorrhage.

Medical measures which have been used include the administration of iodine preparations, and radioactive I^{131} in cytonecrotic doses. The former have been unsuccessful in materially reducing the size of the mass, and the latter, by destroying all thyroid tissue present, predicates oral thyroid substitutes.

Early surgical measures such as cautery and multiple circumferential ligature were often incomplete and sometimes fatal. Before thyroid extracts were available they offered a dubious benison; the relief of oropharyngeal symptoms at the price of myxoedema.

Deliberate partial removal of the lingual mass offers no solution. There are theoretical advantages in leaving sufficient thyroid tissue to maintain normal function while removing the source of obstruction. In practice it is difficult to estimate at operation the amount to be left, and subsequent hyperplasia in response to physiological demands leads to increase in bulk with reappearance of obstructive symptoms (Ackland, 1955).

In the case reported here the concentration of 4-5% μc. of I^{131} in the tongue five weeks after operation indicates incomplete removal of the ectopic thyroid. The absence of a capsule in this case renders this likely. It is fortunate that secretion in the autograft has been adequate, for if otherwise, the lingual residuum might have attained an appreciable size. Two years after operation the tongue is normal in appearance.

Pathology. Several patterns of cellular arrangement have been observed in lingual ectopia of the thyroid. The commonest is that of a normal thyroid gland, followed next by the 'foetal adenoma' type; colloid and hyperplastic (thyrotoxic) types occur less often.

Almost from the beginning the pathological descriptions have been haunted by the spectre of malignancy arising in the ectopic thyroid tissue, and on the degree of probability of this hinges the permissibility of autotransplantation.

Montgomery (1936) concluded that of eight cases of supposed malignancy in a series of 144, only four warranted serious consideration. He noted that all four occurred in middle-aged males and that no proven case of carcinoma of a lingual thyroid had been reported in the female.

Wapshaw (1942) in a further review reached the same conclusion, the sole exception being one case which was complicated by the presence of orthotopic thyroid tissue with the possibility of neoplasia arising within it.

In the great majority of suspect cases the presumption of malignancy has been based on the microscopic appearances and not on the clinical course.

There are undoubted difficulties in arriving at a correct diagnosis of malignancy in thyroid tissue which has a well-deserved reputation for being misleading. At one extremity of the morphological spectrum, which carcinoma of the thyroid gland presents, there is a mature and fully differentiated cellular picture, as the discarded terms 'lateral aberrant thyroid' and 'benign metastasizing struma' bear witness. Delay in the appearance of metastasis for decades is well recognized. On the other hand the wild cellular proliferation of some benign hyperplasias may strongly suggest malignancy which is not confirmed by the clinical course.

The frequent absence of a capsule separating the lingual ectopic thyroid tissue from the substance of the tongue is an accepted fact, and the consequent lack of a plane of cleavage leads to the appearance of fragments of thyroid tissue scattered among muscle fibres at the margin of the operative specimen. This has often been misinterpreted as 'capsular invasion' and 'local malignancy'. Subsequent local 'recurrence' after excision of lingual ectopia may well be due to the proliferation of these scattered cells in response to the physiological stimulus of the ensuing hypothyroid state. The embryological development of the thyroid gland and its well-documented anomalies make it likely that fragments of thyroid tissue litter the trail of migration.

The rarity of lingual ectopia, the paucity of long-term follow-up reports and the infrequent attempts at autotransplantation have not provided sufficient evidence hitherto to permit definite conclusions. When all these factors are taken into account the sum of evidence does not appear to be sufficient to prohibit autotransplantation.

Surgery of Access. Several operative approaches have been described. The simplest and most direct is the oral route which has been used since the earliest recorded attempts at surgical relief, the technique evolving from cautery through multiple circumferential ligature to a more precise excision. While some cases lend themselves readily to this approach, others present difficulties which have led to extension of the oral route, to include mandibular osteotomy, incision of the cheek, and splitting of the tongue. These unattractive modifications are avoided by access to the tumour from below the mandible.

Two inframandibular approaches have been described. An anterior suprahyoid or transhyoid pharyngotomy requires a dissection through the body of the tongue (Bocca and Marinoni, 1951). Theoretically the exposure gained is a limited one and has the disadvantage of traversing a vascular organ before reaching the tumour.

Lateral pharyngotomy, first described by Lympius (1897), has been recorded on six occasions in the literature by Lenzi (1905), Gachet (1912), Owens (1926), Ward *et al.* (1954), and Ackland (1955). In the case presented here lateral pharyngotomy was entirely satisfactory. The exposure was generous and control of half the vessels to the tumour (the right lingual artery and veins) was effected before excision was commenced. The tumour was displaced into the wound and dealt with in full sight. Reconstruction of the strata of the wound was a simple matter and infection due to opening the pharynx was prevented by chemotherapy.

Autotransplantation. Transplantation of the excised thyroid tissue has been attempted in a small number of cases and has met with variable degrees of success. Two cases (Bocca and Marinoni, 1951; Lawson, 1957), have been successful as attested by I^{131} surveys, and a third is reported here. Buckman (1936), Ray (1938), Wapshaw (1942), reported failure in their cases, and Swan, Harper and Christensen (1952), after early promise of success, observed ultimate lack of adequate function in the grafts.

Subsequently Swan *et al.* (1952) conducted a series of laboratory experiments which have contributed greatly to the success of recent attempts. Their conclusions were:

1. The optimal thickness of tissue slices to be grafted is 1-2 mm.
2. The recipient site is relatively unimportant. Muscle and subcutaneous tissue are suitable and accessible.
3. At least two recipient sites should be used, as initial infection and subsequent injury may destroy a single graft.
4. A lag of at least four months is to be expected between implantation and detectable function. The cells of the graft appear normal during this period. Lawson (1960) has noted recurrent swelling and tenderness at the site of the autograft during the menstrual cycle and though this has not yet appeared in the patient whose case is reported here, consideration should be given to this possibility in selecting the donor site; this should take into account all foreseeable fashions in clothing and should not be constricted by an elasticized waist band. The mid-lower portion of the rectus muscle fulfils these desiderata, though the left side might be preferable.

Withholding thyroid preparations during the post-operative phase of hypothyroidism (Stone, Owings and Gey, 1934) is a logical principle. It was originated by Halsted (1909) whose experience in the transplantation of parathyroid glands led him to the intriguing concept that a total lack of the relevant tissue and its secretion was a prerequisite for success in grafting an endocrine gland. Though this theory may not be universally true, it is reasonable to invoke the aid of every factor which could favourably affect the result.

Swan *et al.* (1952), from observations on their patient, thought that thyroid extract administered orally suppressed the thyroid stimulating hormone of the pituitary so that hormone production in the grafts diminished. Further, there was evidence that withdrawal of medication released the pituitary

hormone, resulting in a demonstrable increase in activity in the transplant.

In the present instance, after a period of temporary hypothyroidism the patient showed established activity after a lapse of five weeks, and this appears to be the earliest function yet reported in an autograft. Subsequent investigations corroborate the clinical impression that the patient is euthyroid two years later. Successful transplantation enables the patient to dispense with oral substitution therapy which is always available if the graft should fail.

Summary

A case of lingual ectopia of the thyroid gland, excised and successfully autografted, is reported.

The suggestion is made that the term lingual ectopia be reserved for those cases in which I^{131} survey confirms the absence of orthotopic thyroid tissue.

The clinical picture and recommended investigation are summarized.

The surgical anatomy of lateral pharyngotomy and a technique of autotransplantation are described.

The embryology, pathology, indications for operation, surgery of access, and autotransplantation are discussed.

It is a great pleasure to acknowledge my debt to Mr. Robert Lawson whose encouragement and guidance were freely given. I am also indebted to Dr. Alan Williams for the pathological report and slide preparation, to the Thyroid Clinic of the Royal Melbourne Hospital and the Peter MacCallum Clinic for the scintillometer reports, to Mr. E. Thake of the Visual Aids Depart ent of the University of Melbourne for the illustrations and to Dr. Reginald Webster for his help in prepar ion of the final draft of this paper.

This report and the successful outcome have een due to the generous contributions of an anaesth tist, an endocrinologist, a pathologist, a biochemis , a physicist, an artist and a photographer and typist, and their teamwork is gratefully acknowledged.

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JUVENILE FIBROMATOSIS*

A CASE REPORT SHOWING INVASION OF THE BONE

BY

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This paper reports a growth occurring at the angle of the mandible of a 6-year-old boy. The growth consisted of mature-looking fibroblasts with a generous collagenous matrix. The course of this patient up to the present is described as it portrays some of the problems encountered in children with fibrous growths. Despite recent articles on the nature of such growths there remain many instances where it cannot be decided on histological grounds alone whether they are true tumours or fibrous dysplasia. If they are tumours they cannot be separated with certainty into benign and malignant groups by their microscopic appearance. It cannot even be proven whether they are growths of mature fibroblasts, i.e. well-differentiated mesenchymomata, or growths of peripheral nerve cells, i.e. benign schwannomata (neurofibromata). The clinical course of such growths is not totally predictable. Hence the clinician is confronted with the problem of determining how best to manage them; steering a middle course between the Scylla of inadequate and belated removal and the Charybdis of unnecessary mutilation.

Case Report

W.H., a 6-year-old white boy, presented in 1957 with a painless mass at the angle of the right mandible. This mass was thought by his mother to have been present for about six months. She had noted little change in size. On examination the boy was normally developed with no other relevant physical findings and no relevant family or past history. He gave no history of trauma in this area. The mass was approximately 2 by 2·5 cm. and was situated at the angle of the right mandible below and a little anteriorly, deep rather than superficial. It was firm and slightly moveable in relation to the bone. It felt contiguous with, rather than continuous with, the bone. It was painless except for slight soreness on firm palpation. Radiographs showed a spicule of bone on the lower inner border of the mandible at about the site of the mass. No other abnormalities were seen. The chest was clear and blood and urine analyses were normal. On July 6, 1957, the mass was explored through a crease incision in the neck below the mandible. It proved to be ill-defined, whitish, firm fibrous tissue resembling a deep scar. A biopsy was taken and the frozen section reported as 'neurofibroma—benign'. The remaining portion of the mass, which extended posteriorly to the upper part of the sternomastoid muscle, deeply into the parotid gland and anteriorly into the submaxillary gland, was removed piecemeal. The bone spicule noted in the radiograph was found in the deep part of the mass and removed. Unfortunately the cervical branch of the facial nerve was injured and a weakness of the corner of the mouth ensued. Recovery was otherwise uneventful. The permanent sections were considered to confirm the diagnosis of benign neurofibroma.

Three months later there was no palpable mass in the area. Within a year a recurrence was noted. In August 1958, the mass was 2·5 by 3 cm. in the same location as before. It felt as before though it seemed more firmly fixed. Radiographs of the mandible showed a slight depression where the spicule had been removed and an area of rarefaction about 1 cm. in diameter near this site. A radiograph of the chest was clear.

In September 1958, a wide block dissection of the mass was performed. The previous scar was excised, although it was below the recurrence. The skin was reflected superficial to the platysma. The block of tissue containing the mass was dissected off the mylohyoid muscle from the hyoid bone upwards. The sternomastoid muscle was not involved and a lymph node in the jugular chain near the mass was removed for section. It was shown to be 'reactive'. After cutting across the inferior part of the parotid gland and freeing the submaxillary gland the mass was free except for its attachment to the mandible. As the angle of the mandible was cut across, after fracturing the outer table, a cavity was opened. This contained a grey homogeneous material. The cut across the mandible was altered to include bone beyond this cavity. The patient made a good recovery. The pathological report was again benign neurofibroma. The grey material within the mandible was histologically identical with that without. On examining the gross specimen it was seen that the mass within the mandible was connected to the larger mass without by a narrow neck of tumour tissue penetrating through an almost microscopic hole in the cortex.

Following this the mass recurred within six months

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

FIG. 1.—Patient showing second recurrence in February 1960.

(Fig. 1). At this time a dimpling was noted in the cheek, appearing like the scar of a penetrating injury. This did not at first seem to be connected to the recurring mass at the angle of the mandible. The recurrence grew slowly becoming more prominent and growing forward and upward until it became continuous with the dimpled area in the cheek. The patient was seen by Dr. A. P. Stout of New York in consultation. He considered that this case fitted into his classification as 'juvenile fibro-matosis'. He considered that the growth was likel to be self-limited and would stop growing if it coul be left long enough. He considered that it was benig and that there was no danger of the cell pattern becomin more malignant or of metastases occurring. Over th next year the mass continued to grow by measuremer and by February 1960, radiographs showed definit evidence of further involvement of the mandible (Figs. and 3). After further consultation with Dr. Stout i was agreed that radical excision was now essentia whether the mass was considered benign or malignan or even simply fibromatosis. This decision was take reluctantly as radical resection entailed removal of large portion of the right mandible. A tube pedicl graft was raised from the right chest in stages and by June 1960, the right cheek and mandible with the mass were resected (Figs. 4 and 5).

Discussion

This case presents the problem of a child with a recurring mass which when excised and examined appeared to be little more than 'scar tissue'. It consisted of mature-looking fibroblasts with elongated pointed nuclei, without evidence of mitoses normal or abnormal, and without palisading. Though some of the nuclei appeared 'wavy' there was inadequate evidence to classify this unequivocally as a schwannoma. There was no demonstrable nervous element in it. This mass had ill-

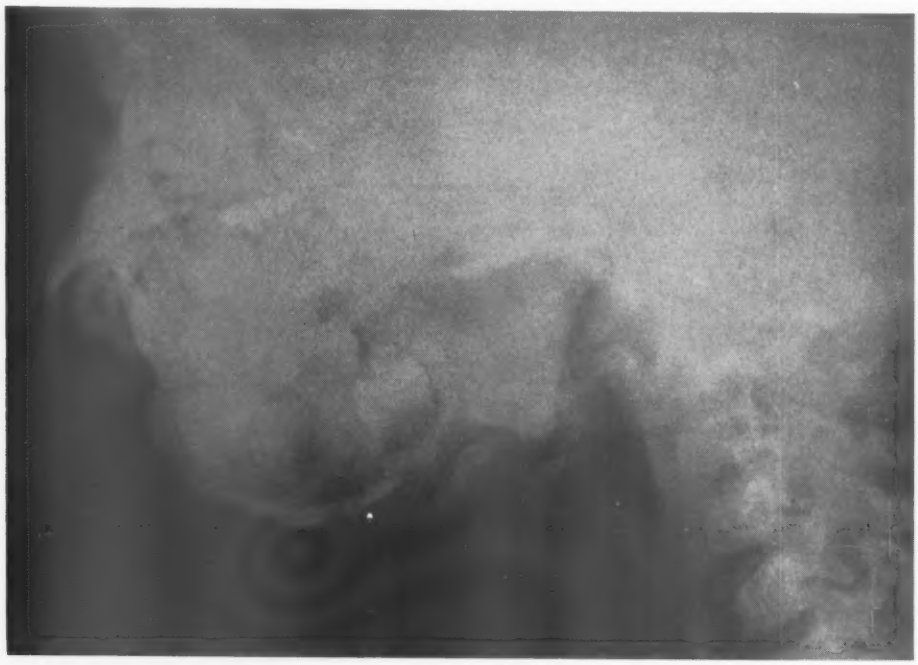

FIG. 2.—Lateral radiograph of right mandible, May 1960, showing involvement of bone.

TABLE

Fibromatoses (tumour-like fibrous tissue proliferation):	
Juvenile fibromatosis:	(*a*) Cutaneous
	(*b*) Deep
Plantar and palmar fibromatosis	
Desmoid tumours	
Progressive myositis ossificans	
Congenital generalized fibromatosis	
Sternomastoid tumour of infancy	
Keloid	
Certain bone lesions:	
Fibrous dysplasia	
Non-osteoid osteoma or non-osteogenic fibroma	
Periosteal fibroma; periosteal desmoids	
Dermatofibrosarcoma protuberans—fibrosarcoma well differentiated (including periosteal and parosteal sarcoma)	
Tumours of the peripheral nervous system:	
Benign	Malignant
Neurilemmoma	Malignant schwannoma
Neurofibroma	
Multiple neurofibromatosis	

FIG. 4.—Patient after operation, June 1960.

defined borders and appeared to be either infiltrating or invading surrounding tissues. By looking at the sections alone and without considering the course and the anatomy of the growth, it would be impossible to state whether it was scar tissue, a desmoid, a neurofibroma or even a well-differentiated fibrosarcoma. A brief classification of growths which may have such an appearance is given in the Table. Most of these are easily classified on their anatomical relations, distribution and clinical course. The present case does not fit any of the types of fibromatosis because of its unique penetration of the bone. Fibromatous dysplasia occurs in the medulla of bone and is what Jaffe (1958) called desmoplastic fibroma. This can only be distinguished from well-differentiated fibrosarcoma by the plumpness and roundness of the nuclei, but this remains within the bone. The periosteal desmoids that Kimmelstiel and Rapp (1951) reported were small lesions eroding the cortex and they did not recur after

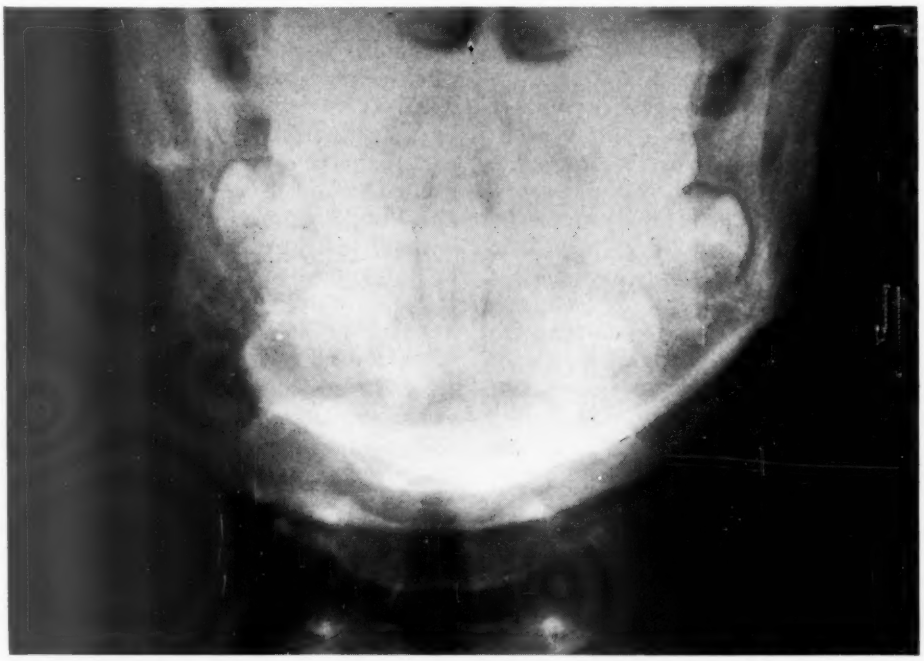

FIG. 3.—A.P. radiograph of mandible, May 1960, showing involvement of bone.

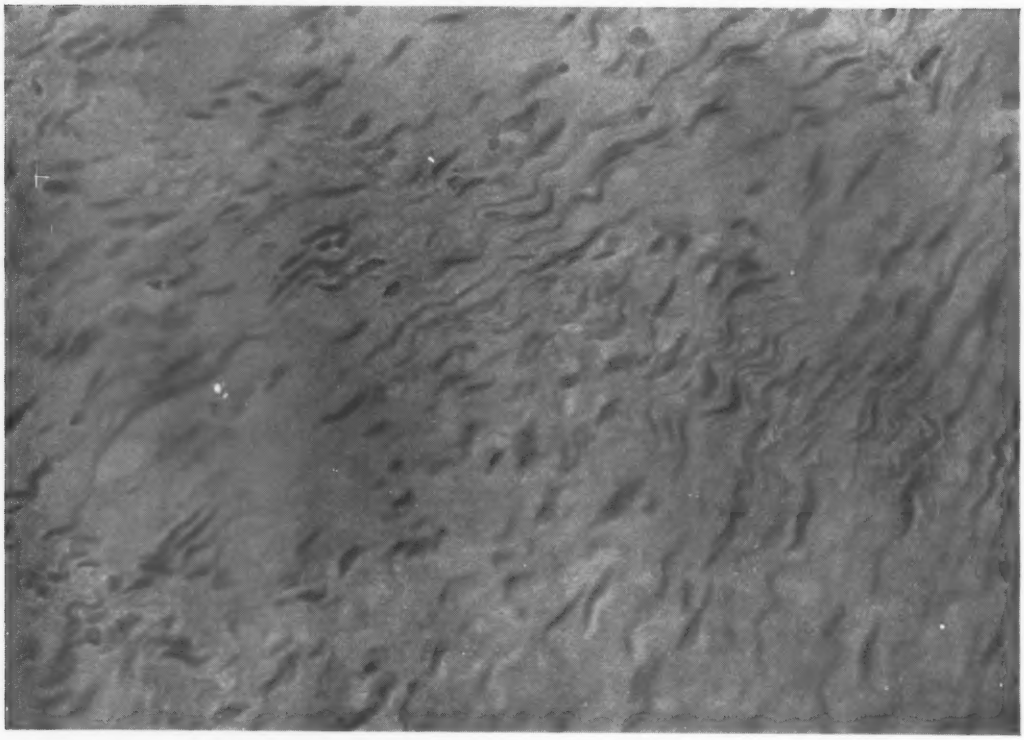

FIG. 5.—Microphotograph from specimen removed June 1960, showing fibrous tissue with generous intercellular matrix. (× 184.)

excision. Nor can it be proved that the periosteal or parosteal fibrosarcoma has invaded the medullary cavity unless the cortex is first destroyed. This lesion could well have started as a periosteal lesion and the presence of a spicule of bone on the mandible when the lesion was first seen is suggestive.

The object of this presentation is not concern over the name that should be applied, but over the best management of such cases. By 'such cases' I refer to children showing areas of desmoplastic hyperplasia no matter in what part of the body they occur. From a study of the cases reported and from talking with Dr. Stout who has been interested in this type of lesion for some time the following conclusions seem justified: (1) The lesion, whether a true tumour or not, does not metastasize; (2) it tends to recur but the cell type remains the same with each recurrence (it does not become less well differentiated); (3) local excision, even piecemeal, may cure the lesion and, this being so, radical excision should not be undertaken at the first attempt, although if it is possible to take a wide margin of normal tissue without undue mutilation, this should be done; (4) recurrence should be treated with wide local excision without lymph node dissection; (5) even such an excision may not be successful and the lesion may kill by local invasion. If the lesion is in the neck, the problem is more precariously balanced because wide excision prejudices vital structures, but recurrences may, as in this case, require even more mutilating surgery. Stout (1954) reported six cases of juvenile fibromatosis occurring in the neck of children: one was excised piecemeal and did not recur; one was excised in the surgeon's office and did not recur; one was excised, recurred, but then stopped growing without further treatment; two were excised, recurred, but were cured by re-excision; one was excised, recurred and it was impossible to re-excise; it killed by local invasion.

Radiotherapy seems to have had little effect on these lesions, but it should be borne in mind that fibrosarcomata have been reported in areas that have been radiated some time previously. More interesting are the possible effects of hormones. Much experimental work has been done by Lipschütz and Vargas (1941) and Lipschütz and Grismali (1944) who showed that oestrogens were fibromatogenic in guinea-pigs and that progesterone and certain adrenal cortical steroids were anti-fibromatogenic. A recurring abdominal desmoid in a 2½-year-old girl has been treated with cortisone

by Panos and Poth (1959) with apparent success. Bullock (1955) mentioned using testosterone in a 21-year-old woman with a recurring extra-abdominal desmoid starting in the trapezius which involved many structures, including the carotid sheath. He thought that it induced some control of the growth. The idea of controlling desmoplastic hyperplasia with steroids deserves more study.

Summary

A case of fibrous tissue growth occurring at the angle of the mandible in a 6-year-old boy and recurring after excision is reported. This case was unusual in that the mandible was not only eroded at the second recurrence but that the medullary cavity was invaded at the time of the first recurrence. The nature and management of desmoplastic growths are briefly discussed.

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THE SCOTTISH PAEDIATRIC TUMOUR REGISTRY*

A Report on the First Five Years: 1955-59

BY

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The Scottish Paediatric Tumour Registry was organized by the Scottish Surgical Paediatric Club and began to operate on January 1, 1955. The Scottish Paediatric Society promised their co-operation and it was thus assured of support from paediatric surgeons and paediatricians in the five Hospital Regions of Scotland. Co-operation was sought from pathologists in all hospitals with paediatric units, and these have supplied pathological material to the Registry. A panel of pathologists has been formed to whom difficult cases are submitted for an opinion. This panel consists of one or more pathologists from each region, these being paediatric pathologists if available, otherwise the pathologists mainly responsible for paediatric pathology in their regions. The follow-up of patients has been conducted by means of forms requesting a report, which are sent out from the Registry for each patient on the live register at six-monthly intervals. The Registry has lacked the advantage of a whole-time worker who could visit hospitals to examine records and call on defaulting patients in their homes. Nevertheless, the simple method adopted has worked surprisingly well, and few patients have been lost sight of and very few indeed of those with malignant tumours.

This communication deals with only one aspect of the information that is being collected by the Registry: the outcome of the malignant cases as ascertained by the follow-up to date (July 1960). For this purpose all malignant and borderline cases registered up to December 31, 1959, have been reviewed. The 'borderline' cases were those in which some reasonable doubt existed as to their benign or malignant character, and those that were dangerous to life owing to their situation (e.g. histologically benign astrocytomata) or for some other reason. The malignant and borderline tumours numbered 308, of which the vast majority were obviously malignant. Of the 308, 287 fell into the seven main categories indicated in Table 1, and the following review of outcome includes only these cases.

TABLE 1

MAIN TYPES OF MALIGNANT AND BORDERLINE TUMOURS

Type	No.	Deaths
Leukaemia	79	72
Intracranial tumours	58	33
Neuroblastoma, etc.	53	45
Sarcoma	51	34
Nephroblastoma	32	25
Retinoblastoma	8	2
Hepatoblastoma	6	5
Total	287	216

Of the 287 patients, 216 have already been reported as dead. The leukaemias constitute the largest group. The number of intracranial tumours is smaller than it should be: it is known that many cases from one neurosurgical unit have not been sent to the Registry. 'Neuroblastoma, etc.' includes neuroblastoma, ganglio-neuroblastoma and ganglioneuroma, these all having a common histogenesis though differing in malignancy. The sarcoma group includes all types of sarcoma, Hodgkin's disease and other malignant reticuloses, but not the granulomatous reticuloendothelioses.

Table 2 presents the incidence and outcome of the principal types of intracranial tumours and indicates the much better prognosis of astrocytoma

TABLE 2

INTRACRANIAL TUMOURS

Type	No.	Deaths
Astrocytoma	19	6
Medulloblastoma	15	12
Malignant glioma, etc.	15	11
Others	9	4

* A paper read at a meeting of the British Association of Paediatric Surgeons held in London in July 1960.

TABLE 3
SURVIVAL TIME IN 49 CASES OF INTRACRANIAL TUMOURS

Time (yrs)	Astrocytoma		Medulloblastoma		Malignant Glioma	
	Alive	Dead	Alive	Dead	Alive	Dead
<1	2	4	—	9	2	7
1–2	2	—	1	3	2	2
2–3	2	1	2	—	—	1
>3	7	1	—	—	—	1
Total ..	13	6	3	12	4	11

compared with the other types. Table 3, in which the times of survival of patients with intracranial tumours are shown, confirms the relatively favourable outcome of astrocytoma and the unsatisfactory outcome of the other types. The absence of survivors of medulloblastoma beyond the third year is particularly disappointing.

TABLE 4
NEUROBLASTOMA, ETC.

Type	No.	Deaths	Survival Time (Eight Cases)		
			< 1 yr	1–2 yrs	> 2 yrs
Neuroblastoma and ganglioneuroblastoma	51	45	3	1	2
Ganglioneuroma ..	2	0	—	—	2

Table 4 shows the outcome of tumours of the sympathetic nervous system. The two ganglioneuromata were regarded as probably benign. The other 51, whether neuroblastoma or ganglioneuroblastoma, were regarded as fully malignant. Only six of these survive, of whom only two have survived more than two years. Of those who died, only one survived more than one year.

Table 5 shows the outcome of a small series of cases in which vitamin B_{12} was used in treatment. The number is too small and the outcome too equivocal to allow conclusions to be drawn, but some encouragement may be drawn from the fact that the only two patients who have survived for more than two years are in this group.

TABLE 5
VITAMIN B_{12} THERAPY IN SEVEN CASES OF NEUROBLASTOMA

Age	Alive	Dead	Survival Time
4 mths	+		9 mths
6 mths		+	10 mths
9 mths	+		3½ yrs
1 yr		+	6 mths
2 yrs	+		2½ yrs
5 yrs		+	2 mths
9 yrs		+	8 mths

Tables 6 and 7 show the incidence and outcome of the main types of sarcoma. Lymphosarcoma was the most frequent type and had a very unfavourable outcome, only one patient having survived more than one year. Fibrosarcoma compared favourably with the other types, there having been only one death among nine patients, four of the survivors being well after more than four years.

TABLE 6
SARCOMA (MAIN TYPES)

Type	No.	Deaths
Lymphosarcoma	14	11
Reticulosarcoma, etc.	13	9
Fibrosarcoma	9	1
Myosarcoma	4	3
Osteosarcoma	4	3
Total	44	27

TABLE 7
SURVIVAL TIMES IN 36 CASES OF SARCOMA

Time (yrs)	Lymphosarcoma		Reticulosarcoma		Fibrosarcoma	
	Alive	Dead	Alive	Dead	Alive	Dead
<1	2	11	1	4	3	0
1–2	0	0	1	0	0	1
2–3	0	0	0	2	1	0
3–4	0	0	1	1	0	0
>4	1	0	1	2	4	0

TABLE 8
SURVIVAL TIMES IN 32 CASES OF NEPHROBLASTOMA

Time (yrs)	Alive	Dead
<1	1	20
1–2	1	3
2–3	4	2
3–4	1	0
Total ..	7	25

Table 8 shows the outcome of the 32 cases of nephroblastoma and presents an unexpectedly gloomy picture. It confirms the general impression that most fatal cases terminate within a year, but there were five deaths after that period, two being during the third year after treatment. These results are worse than those of many published series of cases, but it may mean only that a larger number is needed to give a just indication of the prognosis of nephroblastoma.

BRITISH ASSOCIATION OF PAEDIATRIC SURGEONS

The Seventh Annual Meeting of the British Association of Paediatric Surgeons took place at The Hospital for Sick Children, Great Ormond Street, London, on July 6, 7 and 8, 1960, under the chairmanship of the President of the Association, Mr. David J. Waterston. Surgeons from Great Britain and 20 overseas countries attended the meeting. Three mornings were reserved for lectures. On two afternoons colour television of operations performed by the surgeons at The Hospital for Sick Children was relayed to the Lecture Theatre of the Nurses' Training School. The President gave a Reception on the evening of Wednesday, July 6, which was attended by all members and guests, and the Annual Dinner took place on the evening of July 8.

It was decided to hold the Eighth Annual Meeting in September 1961, in Stockholm.

The following are abstracts of papers not published in full:

G. HYDE (Liverpool and New York). 'A Study of Possible Aetiological Factors in the Development of Sclerema in Newborn Infants following Operation, with particular reference to Temperature Regulation.' Twenty infants were selected for study from admissions to the Neonatal Surgical Unit, Alder Hey Children's Hospital, Liverpool (neurosurgical cases were excluded).

The following investigations of temperature control were carried out:

(1) A careful estimation was made of the duration of transport and the environmental temperature during transportation in order to evaluate hypothermia or lack of hypothermia induced by transporting the infant to the hospital.

(2) Skin and rectal temperature readings were tabulated during surgery; and the time needed postoperatively to bring the infants' temperature back to normal was recorded.

An estimation was made of the infants' fluid balance.

Biopsies of the skin and subcutaneous fat were taken from operative wounds and from multiple areas immediately after death in order to determine the histological features of sclerema.

F. DOUGLAS STEPHENS (Melbourne). 'Vesical Diverticula in Children.' Diverticula of the bladder occur with and without associated urethral obstruction. Only the non-obstructive types were included in this paper.

Nine patients exhibiting non-obstructive diverticula were studied. Two types, excluding urachal anomalies, were observed:

(*a*) The common narrow-neck type, and

(*b*) The uncommon wide-neck type.

The narrow-neck diverticula were frequently paraureteral. They had an intimate relationship with vesico-ureteral reflux.

The wide neck diverticulum occupies the side wall of the bladder; it is an anomaly which is not commonly recognized; and a new type of surgical repair was described.

Also considered were (i) the diverticula, their pathology and their surgical management, and (ii) the association of vesico-ureteral reflux with the diverticula and the aetiology of this reflux.

R. T. SOPER (Liverpool and Iowa). 'The Management and Unpredictable Prognosis of Wilms' Tumour Metastases.' Since 1948, 27 cases of nephroblastoma have been treated in Liverpool; 14 of these are known to have died of metastases. Seven cases have been selected for this paper because of metastases which appear to have been treated successfully.

Five cases had pulmonary metastases, and the treatment of secondary growths in the lungs was discussed in some detail. In one case there were massive metastases in the lymphatic and venous systems, and one child had liver metastases, Four of these children survived for periods of between 18 months and 11 years after treatment of their secondaries. Two children died of post-irradiation pulmonary fibrosis, necropsy showing no residual neoplasm. In one recent case the hepatic secondaries disappeared after a course of chemotherapy.

J. LISTER (London). Work carried out with Dr. Philip Callaghan in Dr. Henry Swan's department of surgery in the University of Colorado was reported.

Dog blood was exposed in a disc oxygenator to gas mixtures containing various tensions of carbon dioxide at varying temperatures, and haemoglobin dissociation curves plotted. It was shown that increased carbon dioxide tension opposed the shift of these curves produced by hypothermia. The carbon dioxide tensions required to produce this effect produced bubbling on warming and it was thought some other method of acidifying the blood would be required for clinical use.

E. M. O'NEILL (Sheffield). 'A Method for Predicting the Eventual Head Size in the Early Stages of Infantile Hydrocephalus.' The correction of progressive hydrocephalus must be carried out early in the disease process if it is to be effective, but in choosing cases for surgery it is necessary to exclude those cases in whom early spontaneous arrest of rapid head growth will take place. A method of doing this has been evolved; the technique depends on the comparison of rates of head growth in these patients with those of normal children. The method is graphic, simple to apply and because of its incorporated detail the approximate head size at 1 yea

can be forecast whilst the child is still under the age of 4 months, and in many cases long before this.

When the method was applied to a retrospective series of 99 cases it was found that a correct prognosis for the approximate head size, according to one of three grades, could be made in 90% of them. Of even greater importance was the finding that it was possible to make this forecast four or more weeks before 74% of the most severe cases could be classified as such, that is, whilst the head circumference was still either normal or only just above normal for the age. When applied to future cases this warning of impending gross head size could allow surgical intervention at a much earlier stage than has been previously possible without operating upon those in whom early arrest of spontaneous hydrocephalus would have taken place.

URINARY TRACT DUPLICATION IN CHILDHOOD

BY

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(RECEIVED FOR PUBLICATION OCTOBER 10, 1960)

The incidence of duplication of the urinary tract has variously been estimated by different authors to be between the extremes of 0·6% (Campbell, 1951) and 6% (Thompson and Amar, 1958) of individuals. The anomaly may remain symptomless and undetected throughout life, but it carries a predisposition to pathological complications, the most severe and urgent of which occur in early childhood, at which age ureteric duplication is not infrequently a urological emergency.

Embryology

Ureteric duplication follows the formation, at about the fifth week of intrauterine life, of an accessory ureteric bud the precise site of origin of which determines the ultimate anatomical features. If the bud arises from the main ureter the final result is an incomplete duplication with the ureters uniting above the bladder; if it takes origin from the mesonephric duct immediately cranial to the main ureter a complete duplication is produced with both ureters opening separately into the bladder. Since the lower end of the mesonephric duct becomes incorporated in the wall of the urogenital sinus the accessory ureter is carried caudally, crossing the main one, and its orifice is found, as a rule, below and medial to the main orifice (Weigert-Meyer law). When the accessory bud arises from the mesonephric duct at a still more cranial site it is carried farther caudally and its orifice comes to lie outside the bladder in that portion of the urogenital sinus which incorporates the mesonephric duct or in the derivatives of the duct itself. Thus, in the male, the accessory ureter may enter the prostatic urethra above the ejaculatory duct or open into the duct, the seminal vesicle or the vas deferens. In the female the orifice may lie in the urethra or in the vestibule adjacent to the urethral meatus; less commonly secondary fistulous communication with the vagina or the uterus, possibly through Gartner's duct, may develop during prenatal life. The accessory ureter most commonly arises from the cranial aspect of the main ureter or of the mesonephric duct and thus makes contact with the cranial portion of the metanephrogenic blastema. As a result, the accessory ureter, the upper extremity of which dilates to form a pelvis without any obvious pelvi-ureteric junction, drains by one, two or three calyces usually the upper third or less of the double kidney. The exterior of the kidney may show no evidence of duplicity or a groove may indicate the division between the two portions. The pelvi-calyceal systems of each part are, as a rule, entirely separate; communication between the two has, however, been described by Beer and Mencher (1938) and by Braasch (1912). Very uncommonly the accessory ureter takes origin from the caudal aspect of its fellow or of the mesonephric duct and so drains the lower portion of the double kidney.

Material

The present review is based on a clinical series of 73 children with complete or incomplete duplication and of nine cases in which the abnormality was a post-mortem finding. Cases of the minimal degree of duplication, e.g. the bifid pelvis, have been excluded and so too have those in which a supernumerary ureter terminated outside the urinary tract or in the lower urethra in the female, i.e. the so-called ectopic ureter, since in this group the symptomatology and the diagnostic problems are quite different. Analysis of the series supports the findings of other authors that duplication, at least as a clinical problem, is commoner in the female than in the male (57 : 25), that it is more commonly unilateral than bilateral (63 : 19), that in unilateral cases each side is more or less equally frequently affected (right 35; left 28) and that in bilateral cases the anatomical pattern is not necessarily symmetrical. Triple ureters were found in two patients and quadruple ureters in one. Associated but unrelated congenital abnormalities of the urinary tract were present in three patients with, respectively, a horseshoe kidney, a large vesical diverticulum of congenital type and urethral valves. Although ureteric duplication is initiated at an early phase of embryonic life the responsible stimulus appears, in most cases, to act locally since obvious extra-urinary congenital

abnormalities were not present in any patient in the present clinical series. Complicated or uncomplicated duplication was found at operation in one patient with exomphalos and at necropsy in six infants with other gross anomalies such as oesophageal atresia, imperforate anus, achondroplasia, myelomeningocele, diaphragmatic hernia and congenital heart disease. In 15 cases the urinary tract duplication was considered to be purely coincidental and unrelated to the patient's symptoms. These children were, for the most part, enuretics or cases of obscure abdominal pain in whom an abdominal radiograph, by showing a large renal shadow, led to intravenous pyelography. Five patients complained of recurrent loin pain on the side of an uncomplicated, uninfected ureteric duplication.

Complications

The main childhood complications of double ureters which are of clinical importance fall into two groups: (1) anatomical lesions consisting of obstructive or non-obstructive dilatation of one or both pyelons, associated with impairment of renal function, urinary stasis and infection; (2) chronic or recurrent urinary infection with a reduplicated but otherwise anatomically normal urinary tract. Patients with structural complications usually present at a much earlier age than those with infection alone. In this retrospective review of cases it was, in some instances, impossible to determine with certainty the precise pathologico-anatomical lesion which was present because of incomplete investigation before excisional surgery, but it has been possible, excluding the indeterminate cases, to recognize certain specific types of pyelonic dilatation, some of which are peculiar to the duplicated urinary tract and some which may also affect the single ureter. In several cases different lesions were present in the same patient.

The Obstructed Megaureter associated with Ectopic Ureterocele. Ectopic ureterocele (Fig. 1), with obstruction of the corresponding accessory pyelon leading to its dilatation and to ureteric tortuosity, was found in 11 instances in 10 patients, three male and seven female. This lesion differs from the 'true' ureterocele which occurs with a single, normally sited ureteric orifice in that it is broader based, usually larger, more centrally situated and the ureteric orifice lies, not at the apex of the cystic protrusion, but towards its lower extremity, at the bladder neck or in the proximal urethra. The orifice may be small and stenotic, as with the true ureterocele, but more frequently it is of normal size or even larger than normal; the obstruction which causes intravesical ballooning of the lower part of the accessory ureter is due to the position of the orifice relative to the vesical sphincter rather than to its size. When the sphincter is in its resting state of tonic contraction it compresses and occludes the termination of the accessory ureter so that the ureter can only empty adequately when the sphincter relaxes during micturition.

The ipsilateral main pyelon was of normal calibre or only slightly dilated with six of the ureteroceles; in the remaining five it was considerably dilated. In four of these the corresponding ureteric orifice was normal in appearance, without, in at least two cases, vesico-ureteric reflux; there can be little doubt that the main pyelon dilatation here was the result of compressive obstruction of its intramural ureter by the ureterocele, particularly since improvement in the degree of dilatation and in radiographic function followed excision of the ureterocele in two cases (Fig. 2a and b). In one patient the twin pyelon had the features of the idiopathic megaureter.

It might be expected that an ectopic ureterocele encroaching, as it does, on the vesical outlet would interfere with micturition and lead to chronic vesical retention of urine. In fact, this occurred in only two of our patients, both male, in whom the bladder was persistently distended, trabeculated and somewhat hypertrophied. Even in these cases the obstructive effects were not particularly severe since, in both, the renal tract opposite to the ureterocele was undilated. The low incidence of dysuria with ectopic ureterocele was also recorded by Ericsson (1954) and by Stephens (1958). It is likely that the emptying and collapse of the ureterocele during micturition are responsible for this relative freedom from urethral obstruction.

The ectopic ureterocele usually leads to symptoms in early infancy; seven of our patients were less than 5 months old. These children were seriously ill with symptoms of vomiting, failure to thrive and apparent pain and all had gross pyuria. In one baby girl the ureterocele prolapsed through the urethra. Intravenous pyelography does not, as a rule, demonstrate the dilated accessory pyelon owing to depressed renal function but the ureterocele may be seen as a round filling defect within the bladder shadow. The ureterocele can usually be seen at cystoscopy, but if it is particularly large it may obscure visibility and render elucidation difficult. The ureterocele is often palpable on bimanual examination of the pelvis under anaesthesia when the bladder is empty.

The Unobstructed Idiopathic Megaureter. The unobstructed or 'idiopathic' megaureter (Stephens,

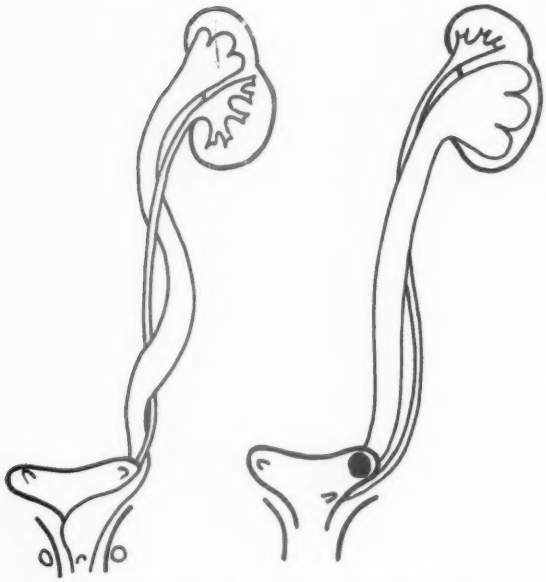
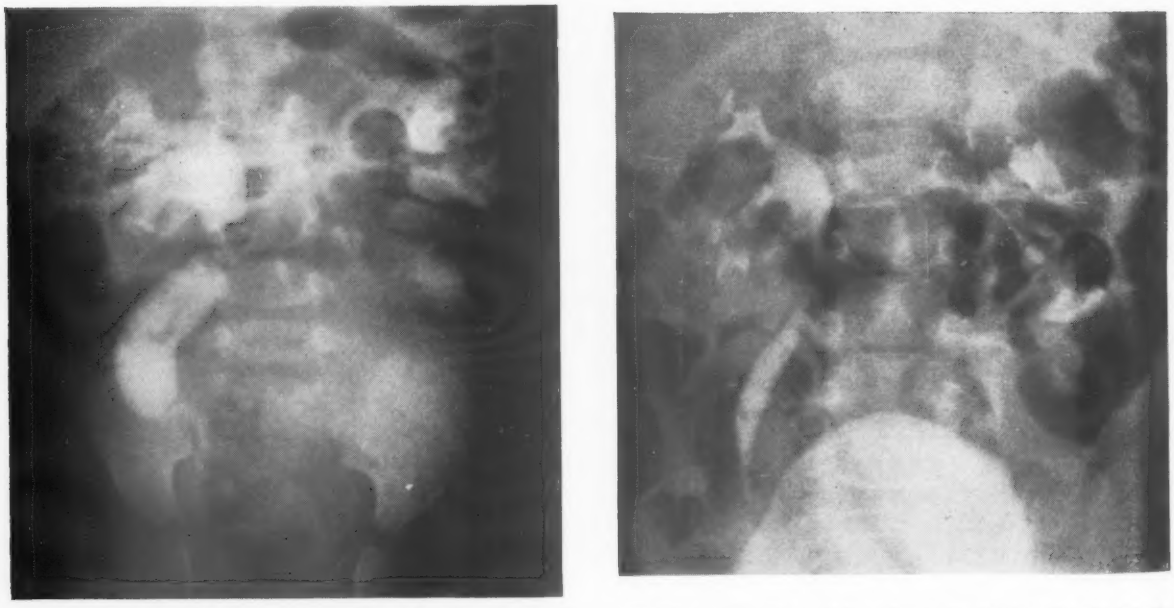


FIG. 1.—Diagram of obstructed megaureter with ectopic ureterocele. The orifice is compressed and occluded by the vesical sphincter.

FIG. 3.—Diagram of the unobstructed idiopathic megaureter affecting the main pyelon.

1956) shows dilatation of the entire pyelon but often little or no ureteric tortuosity (Fig. 3). There is impaired concentration on pyelography. The characteristic feature of the lesion is free vesicoureteric reflux which can be demonstrated at cystography, sometimes during bladder filling, and always during micturition when the ureter and usually also the pelvis and calyces may become markedly distended with dye (Fig. 4); at the conclusion of voiding the ureter empties again into the bladder. At cystoscopy the ureteric orifice is usually seen to be widely gaping but in some cases its dilatation is only apparent during the emission of urine or when reflux occurs with increasing bladder distension. On occasion the orifice, instead of dilating, recedes from the bladder, drawing after it the adjacent bladder wall in the form of a diverticulum. The idiopathic megaureter exhibits variable degrees of dilatation and renal functional capacity, but in the individual case these features remain unaltered with the passage of time, provided infection is controlled (Stephens, 1956); the condition appears to be an inherent anomaly, the result of a developmental defect of the ureteric bud and the related renal parenchyma.

In the well-developed case the diagnosis of the idiopathic megaureter is readily established but its



(*a*) Aged 2 months; before surgery. The primarily obstructed left accessory pyelon does not show. Dilated calyces of the secondarily obstructed left main pyelon are visible. The single right kidney is hydronephrotic and the lumbar ureter is dilated as a result of infection.

(*b*) Six months after excision of the ureterocele. On the left, the accessory pyelon is now visible and the main pyelon, pelvis and calyces are no longer dilated. The hydronephrosis of the right kidney has subsided; slight ureteric dilatation possibly persists.

FIG. 2.—Left ectopic ureterocele; intravenous pyelograms in infant girl.

mildest extreme is difficult to define precisely and different observers have accepted differing diagnostic criteria. In this series only those pyelons showing fairly gross changes on intravenous pyelography and marked distension on reflux from the bladder are considered to be of this type. In some cases of complicated duplication with obvious megaureters, non-distending reflux occurred on cystography into twin or contralateral pyelons which were of normal appearance on intravenous pyelography and it was thought that, in these instances, the reflux was a temporary effect of infection. It is possible, however, that these pyelons represent the minimal degree of the idiopathic megaureter.

According to our criteria for diagnosis, idiopathic megaureter was found in seven patients, each of whom had urinary infection; in three the accessory and in four the main pyelon was involved. The affected pyelon was visible on intravenous pyelography, although with considerably diminished concentration, in three cases; in the remainder it was radiologically silent. The twin pyelon was normal in six cases; in one it was obstructed by an ectopic ureterocele. In two cases there was an ectopic ureterocele on the other side. The age at diagnosis in those patients without associated ureterocele was 3½ years in one and under 6 months in the remainder.

The Simple Obstructed Megaureter. One pyelon in the clinical series had the features of the 'simple' obstructed megaureter of Williams (1958) in which Murnaghan (1957) has demonstrated that the essential pathology is a functional obstruction in the undilated intramural and, in some cases, the lower extramural ureter, because of anomalous muscular patterns in the ureteric wall. In this patient, a boy of 5 years with unilateral duplication, the accessory pyelon was represented by an atretic ureter and a multicystic dysplastic kidney; the main pyelon ureter was dilated and tortuous with a normal, non-refluxing ureteric orifice and, at operation, a short, narrow extra vesical segment. In one necropsy case of incomplete duplication the accessory pyelon was dilated but narrowed just above the point of fusion with its twin and it is possible that this megaureter had a similar pathogenesis.

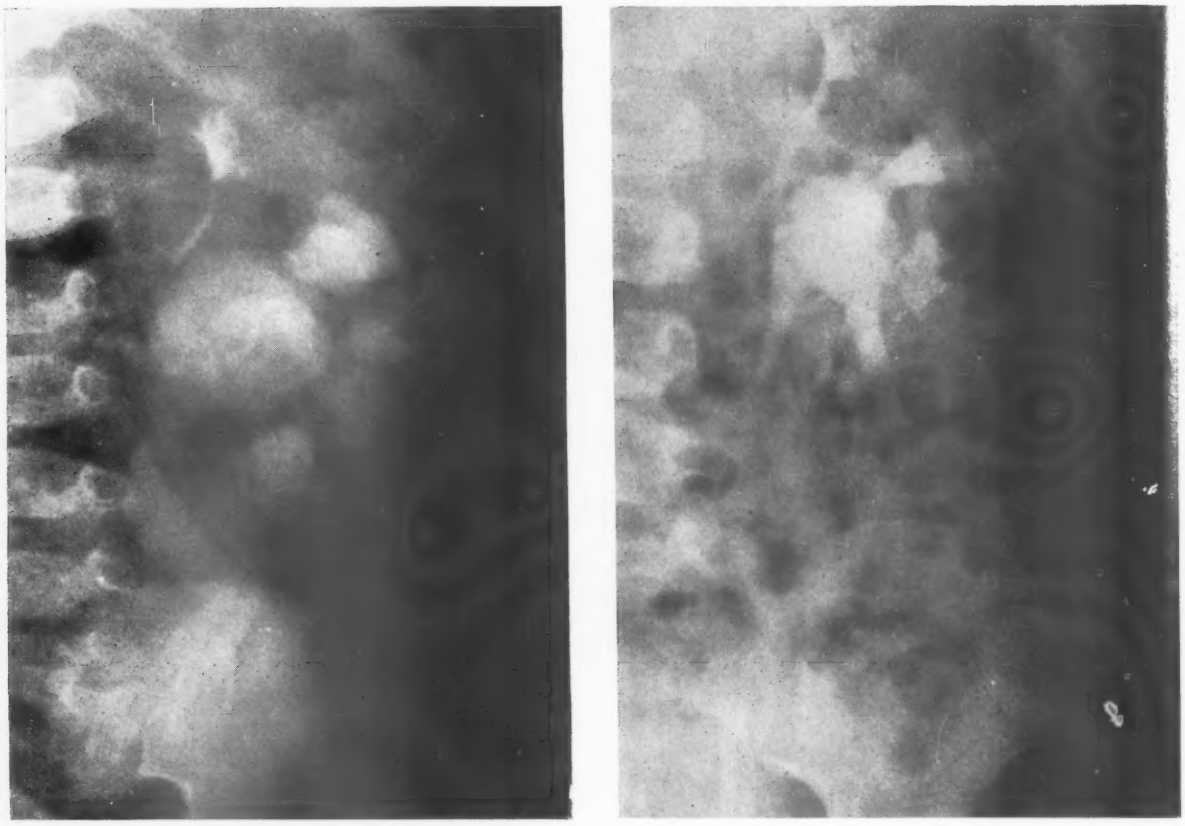
The Infective Megaureter. Both the obstructed and the unobstructed megaureter may, in the young infant, be simulated on the intravenous pyelogram by the effects of urinary infection. At this age infection may lead to marked dilatation of the upper urinary tract, involving the pelvis and calyces as well as the ureter, with delay in ureteric emptying and in some cases, vesico-ureteric reflux. This

FIG. 4.—The idiopathic megaureter. Cystogram in boy aged 7 months, showing reflux into a dilated left main pyelon. This portion of the double kidney was not visible on intravenous pyelography.

infective megaureter can return to normal in respect both of dimensions and of competency of the vesico-ureteric sphincter mechanism (Fig. 5a and b). Since pyuria is present with each type of lesion it may only be possible to distinguish them with certainty by repeated observation after the infection has been controlled.

Pelvic Hydronephrosis. Hydronephrosis due to obstruction at the pelvi-ureteric junction, identical with that which occurs in the single kidney, was found in three clinical cases, children aged 6, 8 and 11 years, and at necropsy of a child who died with multiple abnormalities at the age of 3 days. In each case the main pyelon was affected; the absence of a recognizable pelvi-ureteric junction probably precludes the possibility of this lesion occurring in the accessory pyelon.

Radiology and Diagnosis. Radiography of complete double ureters, particularly when ureteric catheters are in position, shows localized crossing of the ureters in at least one site and sometimes in three and it is often stated that ureters obstruct one another at these points. In no case in the present series was a duplicated ureter dilated to the level of a radiological crossing. When the ureters are exposed at operation it is obvious that they lie more or less parallel to one another and that the



(*a*) Aged 2 months; hydronephrosis and ureteric dilatation affecting the main pyelon.

(*b*) Aged 3 years; the pyelon has returned to normal with the elimination of infection.

FIG. 5.—The infective megaureter; intravenous pyelograms in girl.

localized crossings are more radiologically apparent than real.

In a structurally complicated ureteric duplication there is commonly depressed function of a renal segment with radiological invisibility of the corresponding pyelon; unless the possibility of such a lesion is kept in mind in the child with chronic pyuria and cystoscopy performed, its presence may readily be overlooked. This is more likely to happen when only the larger main pyelon is apparent on intravenous pyelography. Suggestive radiological features in such cases are: an elongated renal soft tissue shadow with the visible upper calyx at a distance from the upper pole, a diminution in the number of calyces as compared with the opposite side or, since a non-visualized accessory pyelon is usually dilated, a lateral displacement of the upper pole of the pyelogram, giving the 'drooping flower' appearance or lateral and sometimes downward displacement of the pelvis and the upper ureter. Occasionally, however, the pyelogram may appear virtually normal. In the type of case with which the present review is concerned double ureteric orifices will almost certainly be seen at cystoscopy and such procedures as perirenal air insufflation, aortography or operative exploration, which are sometimes necessary for the diagnosis of the ectopic supernumerary ureter, will rarely be required.

When structural complications are present, ureteric duplication may present a highly complex picture and, especially in the young infant, it is often difficult to decide at the time of first assessment whether dilatation of a particular pyelon indicates the presence of an intrinsic obstructive or non-obstructive lesion or is secondary to disease of its twin or the result of infection. In such cases the true pathology may only become apparent by observation of the effects of conservative treatment, either surgical or medicinal.

Infection without Structural Complications. Urinary infection in association with complete

or incomplete duplication but without other apparent anatomical anomaly of the urinary tract except, in some cases, slight ureteric dilatation, occurred in 26 children. In 12, 11 girls and one boy, the infection was transient but in 14, 13 girls and one boy, it was chronic or recurrent and, in the latter group at least, presumably associated in many cases with pyelonephritis, although this was proved histologically only in one patient. The age at presentation of these 26 patients was considerably greater than those with structural complications, the average being 6 years. Increased frequency and urgency of micturition, nocturnal enuresis of onset type and attacks of pyrexia, sometimes with loin pain, were the commonest symptoms.

The reasons for the apparent increased liability of the reduplicated but otherwise structurally normal urinary tract to the development and persistence of infection are not known with certainty. Stephens (1956), whose patients were all investigated by micturating cysto-urethrography, found that vesico-ureteric reflux and, in cases of incomplete duplication, uretero-ureteric reflux were commonly present and considered these to be important pathogenic factors. Since vesico-ureteric reflux may be the reversible result of urinary infection, distinction of cause from effect may be difficult and clinical experience suggests that reflux is of significance in the causation of infection only when the volume of regurgitated urine is large so that a large residue of urine remains after micturition. Reflux is, therefore, of great importance in respect of infection with the idiopathic megaureter in which there is a greatly increased ureteric capacity; it is unlikely that reflux into a ureter of normal calibre, even if it causes some ureteric distension, would be of sufficient quantity to be significant. Forsythe and Whelan (1958) found that vesico-ureteric reflux was commonly present in enuretic children without urinary infection. Relatively few of our patients with urinary infection and a duplicated but undilated urinary tract underwent cystography so that the incidence of ureteric reflux in these cases is not known. Reflux was, however, not present in the patient with histologically proven chronic pyelonephritis; in this 6-year-old girl the disease, obvious on intravenous pyelography because of delayed concentration, small size and approximation of calyces, was confined to the lower portion of a completely reduplicated right kidney.

Wayne (1959) noted that, in patients with infection and ureteric duplication, retrograde pyelography suggested ureteric stasis as dye was still present in the pelvis or ureter 10 minutes after the injection. Image intensifier studies in five of our cases have, however, shown no delay in the emptying of undilated duplicated ureters.

The predisposition of the congenitally hypoplastic, dysplastic kidney to infection is well recognized. This anomaly, indistinguishable radiologically and macroscopically from the scarred hypotrophic kidney of chronic pyelonephritis, is identifiable histologically mainly by the presence of primitive tubules, resembling those of the foetal kidney, which have a wide lumen and a lining of deeply staining cubical cells, surrounded by a concentric arrangement of loose connective tissue which may contain angiomatous material and cartilage. The frequent association of gross dysplasia with pyelonephritis raises the question whether lesser degrees of dysplasia may predispose to the development of pyelonephritis in a kidney which appears normal radiologically. Marshall (1953) considered that persistent foetal elements in the renal parenchyma constitute *loci minoris resistentiae* to infection and Ericsson and Ivemark (1958), who were of the same opinion, found such elements to be present frequently with complicated ureteric duplication.

Histological material was studied from the parenchyma of 42 pyelons from the entire present series. Undoubted dysplastic tissue was found in ten. In only one of these was the corresponding ureter of normal calibre; the remainder was associated with hydronephrosis and obstructed or unobstructed megaureter or, in one instance, with an atretic ureter. In 20 specimens the renal parenchyma was histologically normal; in 15 of these the ureter was normal and in five it was dilated. Chronic pyelonephritis without dysplasia was found in 12 specimens; in one the ureter was normal and in the remainder it was pathologically dilated. Many of these last sections showed marked fibrosis and distortion of renal tissue and it was considered possible, in some instances, that dysplastic elements might have been present initially, but subsequently became obscured by scarring. In the majority of cases in which a histological specimen was obtained from a renal segment drained by a normal pelvis and ureter there were marked pathological changes in the twin pyelon; no definite conclusions can be drawn from this series, owing to the paucity of histological material from a duplicated but otherwise anatomically normal urinary tract, concerning the part played by dysplastic elements in predisposing to infection in such cases. It is apparent, however, that the renal parenchyma is frequently normal when there is no dilatation of the corresponding pyelon and that dysplasia is usually associated with megaureter and hydronephrosis, as it was in 10 of Marshall's (1953)

12 cases. In the latter instance it is likely that the urinary stasis resulting from the dilatation of the pyelon is of greater significance in the pathogenesis of infection than the parenchymal anomaly.

The embryological sequence of events which associates a congenitally abnormal ureter with an abnormal renal parenchyma probably differs with the type of lesion. An inherently defective ureteric bud may induce the formation of a defective kidney or vice versa and it is likely that the non-progressive idiopathic megaureter constitutes such a primary defect of germ plasm. The kidney parenchyma in three of our six cases, from which histology is available, contained dysplastic tissue and it was considered to be present possibly in a further one. With the obstructed megaureter the ureteric and renal anomalies may both be the result of obstruction; renal dysplasia is not uncommonly found with the dilated urinary tract resulting from urethral valves. A urinary obstruction present at an early period of foetal life appears to interfere with the maturation of the developing nephrons and also with the development of the ureteric musculature; this is of clinical prognostic importance in that, although some improvement in the degree of ureteric dilatation and in radiological renal function may, in some cases, follow the post-natal relief of pre-natal obstruction, complete restoration to normal is never possible. The renal parenchyma from three of our six cases of ectopic ureterocele showed dysplasia and in two others its presence was thought possible; one of the specimens from the two cases of simple megaureter was dysplastic.

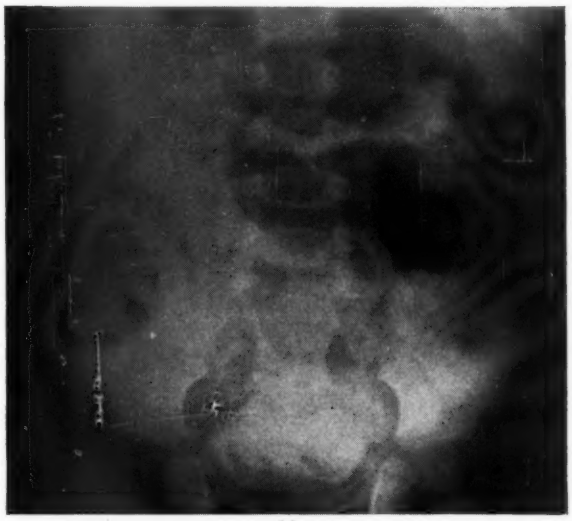
Treatment

The patient with ectopic ureterocele commonly presents in infancy with acute symptoms of urinary obstruction and infection and in these cases the immediate essential is the provision of free drainage of the obstructed ureter into the bladder. Gross and Clatworthy (1950) advocated, for this purpose, a small incision only in the ureterocele wall in order to prevent subsequent vesico-ureteric reflux. It has, however, been our experience, and also that of Ericsson (1954) that, both in the ectopic and the true ureterocele, simple incision does not prevent reflux and it carries the disadvantages that the small opening may diminish in size as the ureter shrinks and also that the residual redundant cyst wall may lead to later complications; in one of our patients it caused a flap valve effect at the bladder neck which interfered with micturition and necessitated a second operation. Excision of the ureterocele by open operation is therefore preferable in that it ensures drainage and carries no disadvantage as compared with incision in respect of reflux. Incision or excision of seven ectopic ureteroceles was performed in the present series. The involved pyelon showed improved function, or visibility for the first time, on intravenous pyelography in three instances (Fig. 2a and b); in all cases pyuria and ureteric dilatation persisted. Ericsson (1954) found similar radiographic improvement, but persistence of infection, in nine of 10 cases. Improved drainage of a secondarily obstructed ipsilateral main pyelon, as shown by improved radiographic function and a diminution in the degree of dilatation, resulted from decompression of the ureterocele in two of four cases (Fig. 2a and b). Some period of time must often elapse before free drainage becomes effective and the time factor may be of great importance when the contralateral renal function is defective or in cases of bilateral ectopic ureterocele. This was exemplified by one patient who required somewhat unorthodox management.

Case Report. J.S., a baby girl, was admitted to hospital at the age of 11 days with pyrexia, vomiting and diarrhoea. Her urine contained a large amount of pus and grew *Esch. coli* and *S. viridans* on culture. Intravenous pyelography showed the faint shadows of bilateral hydronephrotic kidneys. Cystoscopy revealed bilateral ectopic ureteroceles; above each ureterocele was a normal ureteric orifice. There was no reflux into any of the ureters on micturating cystography. At operation, when the child was 4 weeks old, the ureteroceles were excised by open transvesical operation; the right drained through a large orifice into the proximal urethra but no orifice could be found on the left ureterocele. The child's general condition gradually deteriorated after operation; swinging fever and repeated vomiting persisted and she failed to gain any weight. In spite of antibiotic therapy the urine was persistently infected. The blood urea rose to a maximum of 120 mg. %. Intravenous pyelography six weeks after operation showed no concentration by the right double kidney; on the left, only the main pyelon was visible, showing hydronephrosis and a dilated tortuous ureter with marked delay in emptying of the ureter into the bladder (Fig. 6a). Clinically the child appeared to empty her bladder completely. It was apparent that her failure to improve was the result of persistent impairment of drainage of the sole pyelon retaining significant function and that decompression of this pyelon was essential. Tube nephrostomy has, in our experience of such urinary obstruction, been of very temporary benefit only; the presence of an indwelling tube for more than a week or so invariably leads to the exacerbation of infection and to the patient's deterioration. A left cutaneous ureterostomy was therefore performed, both left ureters being divided just above the bladder and brought out in the left iliac fossa (Fig. 6b). The child's general condition showed an almost immediate and striking improvement

(*a*)

(*b*)



(*c*)

FIG. 6.—J.S., baby girl with bilateral ectopic ureteroceles.

(*a*) Intravenous pyelogram six weeks after excision of the ureteroceles. The right pyelons and the left accessory pyelon do not show. Impaired drainage of the left main pyelon persists. Radiograph taken 80 minutes after injection.

(*b*) Temporary left cutaneous ureterostomy. Both left ureters have been divided near the bladder and drain on the surface.

(*c*) Intravenous pyelogram three months after reimplantation of the left ureters into the bladder. Both left pyelons are visible, showing moderate dilatation. Neither right pyelon shows.

and she was discharged home two weeks later on a urinary antiseptic. Intravenous pyelography six months later again showed no dye concentration on the right side. On the left, both pyelons were now visible, each showing moderate hydronephrosis and hydroureter; a small calculus was present in the accessory ureter. The child had continued to pass urine in small quantities through the urethra. Six months after the ureterostomy had been performed the left double ureters were reimplanted into the bladder, bringing them obliquely through the bladder wall in the hope of preventing reflux and the small mobile calculus was removed. Three months after the reimplantation, intravenous pyelography again showed no concentration by the right double kidney; both pyelons on the left showed good concentration of the dye but moderate dilatation remained (Fig. 6c). Six months later the child is well and thriving. Mild pyuria and bacilluria persist in spite of prolonged chemotherapy.

Although radiographic improvement may be apparent after decompression of an ectopic ureterocele, dilatation of the accessory ureter and pyuria almost invariably persist and heminephrectomy and ureterectomy are indicated if the remainder of the urinary tract has returned to normal and the involved pyelon is thus not essential to the patient. Excisional surgery should be carried out as a primary procedure if disease is limited to the one

pyelon and there are no secondary effects on the others. Heminephrectomy or nephrectomy was performed in seven cases in the present series.

Surgery is not required urgently with the unobstructed megaureter associated with duplication; a period of antibiotic treatment is of value, not only therapeutically, but also in allowing a more precise assessment of the pathology and, particularly in the young infant, in distinguishing intrinsic anomalies from reversible effects produced by infection. The treatment of the idiopathic megaureter depends upon its functional capacity and upon the integrity of the remainder of the urinary tract. Excision of the involved pyelon, which was performed in six of our cases, is preferable if it is dispensable because the free vesico-ureteric reflux, as with a large vesical diverticulum, leads to the accumulation of residual urine which promotes infection and endangers not only the anomalous pyelon, but also the others. When retention of the pyelon is essential the residual urine in the ureter and bladder may, in the child of co-operative age, be diminished or even eliminated by having the patient micturate every two hours and, at each occasion, empty the bladder three times at two-minute intervals (Stephens, 1956). By this means and by the prolonged use of urinary antiseptics deterioration in renal function may be prevented. Plastic operations at the uretero-vesical junction such as those described by Bischoff (1957) and by Hutch (1952), which aim at preventing vesico-ureteric reflux, have not been employed in any case in this series but they have, in our experience, been applied with success to the idiopathic megaureter involving a single pyelon; it appears likely that, with slight modification in technique, they could be used for the duplicated ureter.

Heminephrectomy presents few technical problems in cases of ureteric duplication. The line of division of the kidney may be apparent as a groove on the surface; frequently the diseased portion is firmer to palpation than the normal or is hydronephrotic so that it is nearly always possible to excise one pyelon without opening the pelvi-calyceal system of the other. It is important that the ureter is completely removed; a residual stump of ureter, not only in the case of the idiopathic megaureter but also in that of the ectopic ureterocele, particularly if the ureterocele has previously been incised or excised, acts as a diverticulum, leading to the persistence of infection and possibly, as occurred in one of our cases, to calculus formation. The double ureters often share a common wall in the lowest inch or two and, in order to avoid injury to the twin ureter or to its blood supply, only that part of the diseased ureter which is unattached to its twin must be resected, leaving the common wall intact; the resulting small aperture in the bladder at the site of the ureteric orifice requires a suture.

The simple megaureter did not present as a clinical problem in the present series. When it does so, treatment depends upon whether the involved pyelon is dispensable or must be retained. In the latter instance reimplantation of the ureter into the bladder or uretero-ureterostomy (Rothfeld, 1960) may be indicated.

The treatment of hydronephrosis due to obstruction at the pelvi-ureteric junction is the same in the duplicated kidney as in the single organ. In one of our cases pyeloplasty was performed; in the others, nephrectomy or heminephrectomy.

In the treatment of loin pain associated with uncomplicated ureteric duplication, Gutierrez (1944) recommended upper segment heminephrectomy in the adult because of presumed 'impaired ureteric dynamism'. This procedure has little or no justification in the child. In our five patients with loin pain the symptom was only occasional and did not appear to be severe.

The treatment of the older child with chronic or recurrent urinary infection associated with ureteric duplication, but without complicating hydronephrosis or megaureter, differs little from that of the patient without duplication; it consists mainly in the prolonged administration of urinary antiseptics and the prevention of reinfection by the avoidance of constipation, the elimination of obvious septic foci and, in the girl, local cleanliness. Gross (1953), in the belief that duplicated ureters are mutually obstructive, advocated upper segment heminephrectomy and ureterectomy in order to promote drainage from the lower and larger portion of the kidney. Unless, however, impaired ureteric drainage can be demonstrated radiologically, and this was not so in five of our cases of this type examined by the image intensifier, excisional surgery does not appear to be justifiable; its sole indication is in the unusual case in which chronic pyelonephritis can be shown to be confined to a dispensable renal segment. In the majority of children with recurrent urinary infection the attacks tend to cease at about puberty (Williams, 1958), but it must be presumed that each episode is associated with pyelonephritis and with further impairment of renal function. These patients require prolonged frequent supervision; repeated pyelographic examinations, with the object of finding indications for surgery, are of doubtful value. In our experience anomalies such as megaureter and hydronephrosis or pyelographic evidence of hypoplasia or pyelonephritis have always

been present at the initial investigation; we have not observed them develop *de novo* during observation extending, in many cases, over a period of several years.

Summary

A series of 82 cases of ureteric duplication in children is described. The complications found were of two types: first, structural lesions which included ectopic ureterocele, unobstructed idiopathic megaureter, simple obstructed megaureter, infective megaureter and pelvic hydronephrosis; second, urinary infection with a duplicated but otherwise apparently structurally normal urinary tract. The pathogenesis and treatment of the various complications are discussed. Attention is drawn to the value of temporary cutaneous ureterostomy in the treatment of the patient with ectopic ureterocele and secondary obstruction of the main pyelon which persists after decompression of the ureterocele.

I am indebted to Miss Isabella Forshall and Mr. P. P. Rickham for permitting me to include their cases for the purpose of this review, and to Dr. E. G. Hall and Dr. J. Bouton for advice on the interpretation of renal histopathology.

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PAEDIATRICS IN FREETOWN, SIERRA LEONE

BY

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From the Connaught Hospital, Freetown, Sierra Leone

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The Colony of Sierra Leone originated in the sale and cession of a portion of land to Captain John Taylor in 1788 which was placed under the protection of the British Government. The main purpose of the Colony in its inception was to secure a home on the African continent for a number of natives of Africa and some others who, due to various circumstances, had been separated from their countries of origin and were destitute in and about London. Within a few years their numbers had been increased by Africans returning from the New World, notably the West Indies and Nova Scotia. Today 25% of the Africans in the Colony, which now covers an area of 256 square miles, are settlers and their descendants. Apart from these, the African population is tribal, mainly Mende and Temne (Colonial Office List, 1959).

Freetown, the capital, is a seaport with a fine natural harbour and a population approaching 100,000. There are two distinct seasons: the dry season from November to April, and the wet season extending over the rest of the year, the heaviest rainfall occurring in July and August. According to my own rain gauge at Hill Station, a residential area about four miles out of Freetown and 800 feet above sea-level, the annual rainfall varied from 144 to 177 inches during the four-year period that I was in Sierra Leone.

The observations recorded in this paper were made at the Connaught Hospital, Freetown, from October 1955 to September 1959, with a detailed analysis of admissions during the last six months, during which period, through a temporary shortage of staff, I had undivided control of the children's medical ward.

The Connaught Hospital was built in 1912 and although it has a number of unsatisfactory features by modern standards, such as lack of water-borne sanitation, the hospital has served Colony and Protectorate well for nearly half a century. It is a general hospital of about 250 beds, in which there is a paediatric medical ward of 19 cots, an eight-bedded mothers-and-babies ward, and an assortment of side rooms where semi-isolation can be achieved for about six children. In addition there is a smaller ward in the Surgical Unit, but these children have not been included in this paper.

During the six months from mid-March to mid-September 1959, there were 422 admissions to the paediatric medical ward of infants or children under 11 years old. There were 105 deaths, giving a mortality rate of very nearly 20%. Many infants were admitted in a moribund state, and were brought into the Hospital by their parents—not to be restored to health—but that a death certificate might be obtained, thereby pacifying the Registrar of Deaths and facilitating the disposal of the corpse. On these occasions, parental grief at the loss of a child was often masked by a stoical resignation to the inevitable, and there were many instances when I was left with the impression that a child's life was considered of little value, even to the extent that on one occasion the parents were blatantly hostile when an apparently moribund infant was resuscitated successfully. This 'death-certificate-complex' is illustrated in Table 1 where the duration of survival after admission among the fatal cases is recorded. Of 102 fatal cases no fewer than 44 (43%) died within 12 hours of admission, of which 27 (26%) lived less than six hours.

TABLE 1

DURATION OF SURVIVAL AFTER ADMISSION IN 102 FATAL CASES

Duration of Survival: Time after Admission	Nos.
< 6 hrs	27
6–12 hrs	17
12–24 hrs	16
Total in first 24 hrs	60
24–48 hrs	15
3– 7 days	10
In second week	5
> 2 weeks	12
Total	102

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The general pattern of admissions and mortality rates shows similarities with those described by MacGregor (1958) in Ibadan, Western Nigeria, but in his series of 1881 about half were infants under 1 year, compared with only a quarter in the present series. The overall mortality rates of 26% and 20% respectively are both indicative of the unsolved problems facing the health authorities in their task of educating the general population in hygiene and preventive medicine. MacGregor found a constant mortality rate of about 30% up to 6 years and thereafter it fell steeply, whereas in this series the infant mortality rate was just over 40% for the first year, and then fell to about 25% for the next four years, after which there was another sudden fall in the sixth year.

Table 2 shows the number of infants and children in different age groups and the mortality rates among those admitted to the ward. Unfortunately a number of children in the 8-11 year group had to be admitted to the adult wards due to lack of accommodation, and these have had to be excluded from the investigation. The age of the child was usually a matter of speculation by the ward sister and myself as, although the date of birth of a child from Creole families was usually known, those of Temne or Mende stock were rarely remembered or registered.

TABLE 2

AGE OF ADMISSION AND MORTALITY RATES ACCORDING TO AGE

Age	No. Admitted	No. Died	Approximate Mortality Rate (%)
0– 6 mths ..	50	22	44
6–12 mths ..	49	18	37
1– 2 yrs ..	93	28	30
2– 3 yrs ..	58	12	21
3– 4 yrs ..	40	11	28
4– 5 yrs ..	35	6	17
5– 6 yrs ..	24	1	4
6– 8 yrs ..	47	4	8
8–11 yrs ..	26	3	11
Total ..	422	105	20

Although 422 children were admitted, 471 diseases have been recorded. Table 3 indicates the major diseases observed, but it is by no means an indication of all that could have been recorded. Multiple diagnoses are the rule rather than the exception in underdeveloped tropical countries, and only those diseases considered to be a major factor in the child's illness have been included. For instance, a very high incidence of symptomless ascariasis was found, but in only nine children was it considered to be the chief cause of the child's symptoms. Likewise minor degrees (by African standards) of malnutrition and avitaminosis have been ignored, and only where these conditions were the primary cause of admission have they been recorded as such. Indeed, so common was hypoproteinaemia that many children showing oedema of the feet and legs had to be treated as out-patients. This ever-present background of malnutrition in its various forms dominates the practice of paediatrics in tropical Africa.

TABLE 3

THE MAIN CAUSES FOR ADMISSION IN 422 INFANTS AND CHILDREN

Causes for Admission	Cases	Deaths
Pulmonary diseases (non-specific):		
Bronchopneumonia	64	26
Bronchitis	12	—
Lobar pneumonia	6	1
Bronchiectasis	2	—
Total	84	27
Malaria (*P. falciparum*):		
Clinical attack with positive blood slide ..	44	6
Clinical attack with negative blood slide ..	16	1
Cerebral malaria	10	5
Total	70	12
Nutritional diseases:		
Kwashiorkor (hypoproteinaemia)	30	10
Starvation	34	5
Total	64	15
Measles:		
Uncomplicated	20	—
With bronchopneumonia	14	5
With corneal ulcers, iridocyclitis	4	—
With lobar pneumonia	1	—
With encephalitis	1	1
Total	40	6
Dysentery and enteric fever:		
Non-specific	21	9
Bacillary	6	2
Amoebic	2	—
Typhoid	2	1
Total	31	12
Whooping cough:		
Uncomplicated	15	—
With bronchopneumonia	13	2
With encephalitis	1	1
Total	29	3
Tuberculosis:		
Primary complex (uncomplicated) ..	3	—
Segmental or lobar collapse/consolidation	10	—
Bronchopneumonia	2	1
Miliary tuberculosis	5	5
Cavitating disease	2	2
Glandular: (*a*) Cervical	2	—
(*b*) Generalized	2	—
Bone and joint	2	—
Meningitis	1	1
Total	29	9
Tetanus:		
Neonatorum	23	17
Childhood	4	1
Total	27	18
Upper respiratory infections:		
Acute tonsillitis	14	—
Coryza	6	—
Total	20	—

TABLE 3 (*contd.*)

Causes for Admission	Cases	Deaths
Sickle cell crises	9	3
Ascariasis	9	—
Meningitis (pyogenic):		
Meningococcal	2	—
H. influenzae	1	—
Unidentified	3	—
Total	6	—
Dermatological:		
Pyogenic lesions	5	—
Molluscum contagiosum	5	—
Total	10	—
Cardiac lesions:		
Congenital: (*a*) Cyanotic	1	—
(*b*) Acyanotic	3	—
Acquired: Acute rheumatic carditis	1	—
Total	5	—
Infective hepatitis	4	—
Osteomyelitis (acute)	4	—
Poliomyelitis: (*a*) Acute	2	—
(*b*) Longstanding	1	—
Total	3	—
P.U.O.	3	—
Nephritis (Type II)	2	—
Poisoning	2	—
Miscellaneous (chickenpox, microcephalus, polycystic disease of the kidneys)	20	—

Total admissions	422
Major diseases	471
Deaths	105

Clinical Comments

Pulmonary Diseases. The pneumonic diseases were the most frequent cause for admission, particularly in the first and second years of life. Routine blood slides were found positive for *P. falciparum* in nearly 25% of cases. A 'break-through' attack of latent malaria often occurs in acute infections, but in my opinion, the reverse process occurs not infrequently, and a genuine attack of malaria with its rigors, fever, sweating, and chilling of the body can predispose to pneumonia in a child already weakened by infection or malnutrition.

TABLE 4

AGE DISTRIBUTION IN 98 CASES OF PNEUMONIA, INCLUDING 27 ASSOCIATED WITH MEASLES OR WHOOPING COUGH

Age	No. of Patients	Deaths
0– 6 mths	11	5
6–12 mths	18	9
1– 2 yrs	26	12
2– 3 yrs	8	4
3– 4 yrs	9	2
4– 5 yrs	7	2
5– 6 yrs	9	—
6– 8 yrs	6	—
8–11 yrs	4	—
Total	98	34

Throughout the first three years of life the mortality rate for pneumonic diseases was approximately 50% (Table 4), and this was due, at least partially, to the late stage at which the children were brought to the Hospital, many of them in a moribund condition.

Malaria. Despite continuous public health measures to eradicate the anopheline mosquito, malaria is still prevalent in the outlying districts of Freetown and every patient admitted to the Connaught Hospital has a routine blood slide examined for parasites. Positive slides were obtained in 54 out of the 422 admissions with a further 16 in which a firm diagnosis was made on the clinical picture and the response to specific therapy although parasites were not seen in the blood film; this gave a figure of over 16% for all admissions.

P. falciparum was found in all the positive slides in this six-month period, and other species were only rarely reported in Freetown. The absence of *P. malariae* infections has been noted previously (Carter, 1960) in connexion with the comparative rarity of the nephrotic syndrome, whereas a report by Gilles and Hendrickse (1960) showed the high incidence of nephrosis in Ibadan, Western Nigeria, where *P. malariae* abounds. It is now widely accepted that *P. malariae* is one of the aetiological factors associated with the nephrotic syndrome.

Nutritional Diseases. Although placed only third in the general classification, nutritional diseases ranked by far the most important group in the day-to-day ward routine. Patients suffering from pneumonia or malaria usually left the ward, dead or alive, within five days, whereas children with nutritional diseases were often in residence for several weeks or more, and therefore their numbers seemed to swamp the ward. In addition, minor degrees of malnutrition, avitaminosis or anaemia could be detected in a high proportion of children admitted for other complaints and, because it was almost 'normal', such details were rarely recorded in the final diagnosis in the case records. Florid avitaminosis was rare, but minor degrees of ariboflavinosis in particular were common, and from the knowledge of the poor protein intake in most of the child population, subclinical deficiencies relating to the vitamin B group must have been extremely common. One of the more advanced cases of avitaminosis was seen in a 2-year-old child with symmetrical desquamating dermatitis of the dorsum of the hands, cheilosis, and a vivid magenta tongue. It transpired that her mother was one of the hospital dietitians, who had placed her daughter

in the care of her grandmother while she herself went out to work.

Children with hypoproteinaemia showed the classical symptoms of the kwashiorkor syndrome in varying degrees, according to the severity of their protein deficiency; oedema of the extremities, face and trunk; depigmentation of the skin and mosaic dermatoses of the limbs with denuded epithelium in the flexural regions of the groins and genitalia; anaemia, hair changes, lethargy and abject misery; all have been adequately described and all were frequently seen in Freetown. Although the general pattern of the disease appears fairly constant in both East and West Africa, the colouration or discolouration of the hair may be distinctly regional.

In Nairobi, Kenya, I noted that the hair in infants with kwashiorkor was grey and only rarely had a faint ginger tint. On driving from Nairobi to Kampala (about 500 miles), and particularly after entering Uganda, the ginger tint became increasingly common and two or three vivid redheads were usually seen by the roadside before reaching Kampala. In Freetown, the typical colour of the hair in infants with kwashiorkor was an indifferent mouse-brown without any greyness or ginger tint. The texture of the hair appeared similar in each of the three territories, the curly, tightly packed, lustrous black appearance being lost and replaced by straightened, wispy hair, thinned out almost to baldness in severe cases.

The nutritional diseases have been divided into hypoproteinaemia and starvation, and although the two conditions sometimes merged together, it was usually possible to separate them without difficulty. The infant with kwashiorkor receives a diet high in carbohydrate but lacking in protein, while the starved infant receives little of any foodstuff. In the latter case, the infant appears as a wizened object of skin and bone, but otherwise normal in that there are little changes in the hair, which tends to remain dark and curly, and there are no skin changes apart from its laxity. It was found that infants suffering from pure starvation usually responded to treatment more readily than those with hypoproteinaemia, and the mortality rate was less than half that seen among the protein deficient infants.

Diarrhoea and Vomiting. This followed the usual pattern seen in the United Kingdom when associated with a parenteral infection, but the number of acute non-specific intestinal infections (21 cases or 1% of the total admissions) seems remarkably small when the lack of hygiene among the indigenous population is considered. The high mortality rate indicates that only those seriously ill were admitted, and, in fact, lack of accommodation caused many to be treated as out-patients who would have been admitted if cots had been available. In Ibadan, where there was a much higher proportion of infants admitted in general, MacGregor records that 243 out of 1,881 admissions (12·4%) were on account of diarrhoea and vomiting.

Anaemia. Anaemia is not listed among the diseases recorded in Table 3, although by European standards a very high proportion of children had some degree of anaemia. Out of 143 consecutive haemoglobin estimations of children on admission 104 (72·7%) had haemoglobin levels of 70% or less (Table 5). The majority of these was due to iron deficiency; these anaemias responded to oral iron therapy, which was given routinely to all children unless specifically ordered otherwise.

TABLE 5

143 CONSECUTIVE HAEMOGLOBIN ESTIMATIONS MADE AT THE TIME OF ADMISSION

Hb on Admission (%) (Sahli)	No. of Patients
< 30	1
31–40	8
41–50	18
51–60	40
61–70	37
71–80	24
> 80	15

A few of the younger infants appeared to have a normochromic anaemia that failed to respond to any therapy other than blood transfusion.

Tuberculosis. All children with the exception of neonatal infants were Mantoux tested on admission. The injection consisted of 0·1 ml. of a freshly prepared solution of 1 : 1,000 Old Tuberculin. If an indefinite or suspected false negative result were obtained the test was repeated using 1 : 100 O.T. solution. The degree of reaction was observed daily for three days. After excluding those who died or absconded within three days of admission, 222 Mantoux tests were obtained, and the results are recorded in Table 6, together with an assessment of activity of the disease.

There were several notable differences in the pattern of tuberculosis among the Freetown children compared with those I had seen previously in Nairobi, Kenya (Carter, 1954). In Nairobi, there was fever in excess of 102° F. in 14 out of 41 cases (34%) of primary tuberculosis on admission, whereas this degree of fever was not seen in any of

the Freetown children in whom the average temperature was just over 100° F., which is fractionally higher than that seen among children in England (Sheldon, 1943; Paterson and Moncrieff, 1947). Enlargement of the hilar glands was also greater in the Nairobi children where over 54% were considered to have grossly enlarged glands and no case of calcification was recorded. MacGregor considered the hilar glands among children in Ibadan to be slightly larger than seen among children in England, and this was my impression also in Freetown. It was not uncommon to see calcification of hilar glands also. Fibrosis of lung tissue in tuberculosis was never seen in Nairobi children, but two children in the Freetown series who died had extensive fibrocaseous disease of the adult type,

TABLE 6

THE MANTOUX REACTIONS OF 222 INFANTS AND CHILDREN AND ASSESSMENT OF ACTIVITY AMONG POSITIVE OR FALSE NEGATIVE REACTORS

Age	No. of Patients	No. of Positive Reactors	No. of False Reactors	No. with Positive Lesions
1– 6 mths	4	—	—	—
6–12 mths	10	2	—	2
1– 2 yrs	44	3	1	4
2– 3 yrs	46	4	1	5
3– 4 yrs	25	3	—	3
4– 5 yrs	25	—	1	1
5– 6 yrs	17	2	—	—
6– 8 yrs	36	7	—	3
8–11 yrs	15	5	—	2
Total ..	222	26	3	20

one of them being only 4 years old. The general pattern of tuberculosis approximated to that seen in England, which is not surprising, as Freetown, being a seaport and having contact with European countries for several hundred years, has had time to develop a degree of immunity, whereas the hinterland of Kenya has only been exposed to tuberculosis for little more than half a century (Haynes, 1951).

Tetanus. Tetanus was the second greatest cause of death, due largely to the 74% mortality rate among infants in the neonatal period. It has been suggested by MacGregor that the cut umbilical cord is only liable to become infected for a few hours after birth and if this is true the incubation period can be ascertained with reasonable accuracy. Of 23 neonatal cases, only two out of 17 survived among those whose symptoms had started before the ninth day, whereas four out of six survived among those who developed symptoms between the 10th and 14th days (Table 7).

The onset interval, or the time between the first symptom and the first spasm, was not always easy

TABLE 7

INDICATING THE DATE OF ONSET AND FATE OF 23 CASES OF TETANUS NEONATORUM

Day of Onset	No. of Infants	Deaths
4 th	1	1
5 ,,	7	6
6 ,,	4	3
7 ,,	3	3
8 ,,	2	2
9 ,,	—	—
10–14,,	6	2
Total ..	23	17

to assess accurately. The uneducated African mother is very vague in her appreciation of time, but as the first symptom of tetanus neonatorum is the infant's inability to suck (Tompkins, 1958), the mother might be expected to have some idea of the time of onset of the disturbance to this vital function. Tompkins stressed the prognostic value of the onset interval and found that the chances of survival increased steadily the longer it exceeded 24 hours.

Although the number in this series is too small to have any statistical significance, I received the impression that every day the incubation period was prolonged, the chance of survival increased. Even among those who died, death appeared to occur more rapidly and to be more inevitable among those with an incubation period of six days or less than those from seven to 10 days (Table 8). Tompkins had deaths in 79 out of 80 cases (98·7%) where the incubation period was seven days or less, compared with 42 out of 55 (76·4%) where the incubation period was over seven days.

Sickle Cell Crises. The incidence of sickle cell disease and trait in Sierra Leone has yet to be established, but there is little doubt, from the frequency with which the condition is seen in Freetown, that the rate is comparable to that recorded in other West African territories, where figures for sicklaemia have varied from approximately 12% to 23% (Gelfand, 1957a). Nine children were admitted in sickle cell crises during

TABLE 8

SHOWING THE DURATION OF LIFE AFTER THE FIRST SYMPTOMS IN 16 FATAL CASES OF TETANUS NEONATORUM

Incubation Period (days)	No. of Infants	Survival Period After First Symptoms (hours)
4–6	10	7–79 (average 22)
7–10	6	16–96 (average 42)

the six months under review and three of them died.

The clinical features of a crisis have been described by many authors including Gelfand (1957b), Wilkinson (1950) and Blackfan, Diamond and Leister (1944). The usual symptoms described are breathlessness, palpitation, weakness, nausea and vomiting, and pains in the limbs and joints; on examination, there may be jaundice with a variable degree of hepatosplenomegaly, tenderness of the limbs, cardiac murmurs and a severe degree of anaemia. In view of the great variety and inconsistency of the symptoms it is easy to overlook the correct diagnosis unless the possibility of the disease is kept persistently in mind. From my own experience, two patients had appendicectomies performed when they were suffering from abdominal symptoms at the onset of a crisis. One of the children was known to have sickle cell disease, but the symptoms were so suggestive of acute appendicitis that it was considered safer to risk removing a normal appendix rather than leave one that might be about to perforate.

The combination of fever, persistent tachycardia, swollen and painful joints, together with cardiac enlargement and systolic murmurs, caused an erroneous diagnosis of acute rheumatic fever on occasions. The diagnosis can be extremely difficult to make if other signs such as jaundice are lacking, and final confirmation of the disease rests in the hands of those in the laboratory.

Headache is almost always mentioned as one of the symptoms of a sickle cell crisis, but I have failed to confirm this among my patients. Latterly, I came to regard its absence as a point in favour of a sickle cell crisis, and the presence of headache to favour rheumatic fever.

The sites of pain, due to thrombotic emboli of sickled cells are not usually confined to the joints but often involve the long bones also. One boy, aged 8 years, who had had crises every two or three weeks from the age of 18 months, could give early warning of an attack as the pain invariably commenced in the sternum, and within a few hours he had agonizing pain involving all his bones and joints so that he could not tolerate anyone touching him. The severity of the pain that may occur in a crisis does not appear to have been sufficiently stressed in the literature. In several children under my care it was clear that they were suffering excruciating pain as severe as any that I have seen in paediatric practice.

Dermatology. Almost all children go barefoot in Freetown and it is not surprising that infections of the feet were commonplace, but, in general, pyogenic lesions were of a minor degree and only sufficiently severe to require admission on five occasions. The commonest skin conditions seen in the children's ward were those related to the kwashiorkor syndrome.

Molluscum contagiosum was frequently seen, but it was unusual for a child to have more than a score of lesions. The sites most commonly affected lay between the mid-axillary line and anterior axillary fold in and just below the armpit, and on the temporal aspect of the forehead. Lesions were frequently seen elsewhere on the face, neck and thorax, and appeared to select surface areas where the skin was of a delicate texture. It was unusual to find molluscum contagiosum on the back of the trunk or the lower limbs.

Yaws is a condition widespread in the Protectorate of Sierra Leone, but comparatively rare in the Colony area. A Yaws Campaign has been carried out for several years in the Protectorate under the auspices of the World Health Organization, and there is every evidence that it is meeting with considerable success. On my arrival in Sierra Leone in 1955, I was informed that there was no yaws in Freetown, but about a year later, a newly-appointed School Medical Officer, the late Dr. I. Rosanelli, disproved this by producing six children for our inspection; she had found them on routine examination among schools in Freetown.

Congenital Lesions. It is difficult to assess the relative frequency of congenital defects with those seen in England. Certain conditions such as pyloric stenosis appear less frequent and I saw only three Rammstedt operations performed in four years; MacGregor did not see a single case of pyloric stenosis during a year in Ibadan, Western Nigeria. In six months, four congenital hearts were noted among in-patients, and several others were referred to me as out-patients. Also admitted to the hospital was one infant with microcephalus and another with polycystic disease of the kidneys. Only one hare-lip and cleft palate was seen during the whole of my stay in Sierra Leone. I often suspected that infants born with obvious and disfiguring abnormalities might have been the victims of deliberate neglect or even infanticide because of the rarity with which they were seen, compared with the relative frequency of invisible lesions such as congenital hearts.

Rheumatism. Only one case of rheumatic fever was seen in this six-month period. The condition is rare in Freetown and I never saw more than two

cases in any one year. Mitral lesions were found occasionally in the adult population, in whom valvular disease was commonplace, but such lesions were usually due to aortic incompetence of syphilitic origin.

Two children were admitted with Sydenham's chorea in four years, one of them having a severe hemichorea which lasted many weeks. This girl, about 10 years old, developed a systolic murmur in the mitral area shortly after admission, but this faded gradually and was inaudible when I last saw her about one year after the onset of her illness. Chorea must be very rare in Sierra Leone for I showed the child to as many of my African colleagues and nursing staff as possible and none of them had seen the condition previously.

Upper respiratory infections and otitis media were seen much less frequently than in England, and culture of throat swabs almost invariably produced non-specific organisms, haemolytic streptococci being extremely rare.

Virus Infections. Sporadic virus infections were common and there were always patients to be seen in the hospital with infective hepatitis, but we had no outbreak in Freetown of encephalomyelitis such as confronted Rose (1957) in Segbwema in the Protectorate in which nine out of 45 patients were children or adolescents. Acute poliomyelitis was seen occasionally but never in epidemic form. A small outbreak of pleurisy due to a Coxsackie B infection occurred in the summer of 1958, but this was almost confined to young adults.

Methods of Treatment

Transfusions. All transfusions were given by the intraperitoneal route unless some contraindication was present. The technique described by Carter (1953) was used throughout and the only contraindication that occurred was distension of the abdomen by intestinal gas, which was rarely sufficient to necessitate using another method of administration. In these cases and in tetanus neonatorum the subcutaneous route was used in conjunction with hyaluronidase. In infants with acute dehydration the fluids used most frequently were either half-strength Hartmann's solution or half-strength normal saline with 2·5% glucose. Blood transfusions for anaemia and hypoproteinaemia were also given by the intraperitoneal route and the observations made by Macdougall (1958) on the efficacy of this method were confirmed.

Intravenous transfusions were given infrequently and only when they could be supervised personally in view of the danger of the circulation being overloaded. I started using the intraperitoneal method in Kenya in 1952 following two fatal accidents from lack of adequate supervision of intravenous drips, and since then have seen no untoward effects in the course of several thousand transfusions, many of which have been given by the ward sister or staff nurse. I have always been intrigued by the apparent difficulty many Africans have in 'counting against the clock', and this has been true in both Kenya and Sierra Leone. On one occasion when I had started an intravenous blood transfusion in the Connaught Hospital, I was assured by the senior nurse that the drip was running at 12 drops per minute when the actual rate was 92 per minute. MacGregor also records that one or two deaths occurred at University College Hospital, Ibadan, due to cardiovascular effects of transfusion. Apart from the apparent safety and effectiveness of intraperitoneal transfusions, there are the added advantages that the transfusion can be completed within a few minutes and that the child can thereafter be free from restrictions.

Kwashiorkor Syndrome. The usual method of giving a high protein, easily digestible diet was employed at the Connaught Hospital. The standard food used was double-strength skimmed milk, the amount being increased according to the degree of tolerance shown. If the amount was increased too rapidly, diarrhoea often occurred. In addition, intraperitoneal transfusions of blood and/or serum albumen were given. A limited number of 60 ml. bottles of serum albumen (equivalent to the albumen content of one pint of blood) were available, and one bottle was given intraperitoneally on admission. It was unusual to note any marked improvement during the first 24 hours but during the second day a marked diuresis frequently occurred with noticeable reduction in oedema. Unfortunately, only 30 bottles were available, and it was impossible to replace them on account of the very considerable expense involved. The therapeutic value, however, was proved beyond doubt. When the method was first employed I expected to see a transient increase in the size of the abdomen due to the attraction of fluid into the abdominal cavity as a result of using a fluid with such high osmotic power. In actual fact this never occurred and the serum must have been adequately absorbed for diuresis to develop so effectively.

Anaemia. Intraperitoneal blood transfusions were given whenever possible, but for a long time blood was almost unobtainable. West Africans are not enthusiastic blood donors and in Freetown they

usually managed to vanish immediately their blood had been taken for grouping. This was eventually overcome by bleeding the donor before grouping was carried out. Whenever an adult male entered the ward with a child for admission, I guided him to my office and bled him before he had time to cogitate on the prospect. This method increased our supplies of blood at least tenfold, and only on one occasion did I have the misfortune to find I had bled someone who was Group AB. If the blood proved to be incompatible for the donor's own child it could always be used for another infant or infants as there was never a sufficient supply of blood for the ward's requirements. The usual method was to divide a pint of blood between two or three infants and, by using the intraperitoneal route, the whole procedure could be completed in about 20 minutes. If blood were available the transfusions were repeated on two or three occasions at daily intervals.

On one occasion a serious error was made when an infant of about 10 months was given about 250 ml. of Group B blood intraperitoneally, the recipient being Group O. The mistake was not realized until 24 hours later, but the infant showed no signs of an incompatible transfusion and made excellent clinical progress. The fact that the episode did not end disastrously tends to confirm the observation made by Unger (1921) that for infants under 6 months of age any donor is compatible regardless of blood group, and Tallerman (1958), using cells labelled with radioactive chromium, has confirmed that the donor's red cells are absorbed into the circulation following intraperitoneal transfusions.

When malaria was suspected as being a cause of the anaemia the patient was given anti-malarial therapy. Hendrickse, quoted by MacGregor, found antimalarial therapy alone sufficient to restore the haemoglobin level without having recourse to iron therapy or blood transfusion. However, in the few instances when I tried this method I was not impressed by the rate of improvement, and latterly blood transfusion was employed as the main therapeutic measure, its great value being the increased speed with which an infant could be discharged, thereby relieving the strain on the bed situation.

Tetanus neonatorum. All infants were given anti-tetanus serum immediately on admission in dosages varying from 50,000 to 100,000 units, but I have become increasingly sceptical of its value even in those cases where the injection has been given within a few hours of the onset of the first symptoms. Of more than 120 infants with tetanus neonatorum under my care in Freetown I can remember only one instance where A.T.S. was considered to have altered the outcome of the disease favourably. This occurred in a 5-day-old infant, who was given 100,000 units within four hours of developing trismus and before the onset of spasms. In the 15-month period from October 1955 to February 1957, when over 40 cases of tetanus neonatorum were admitted to the Connaught Hospital not a single infant survived. It was during this period that there was an acute shortage of trained nursing staff and the standard of nursing was at a low ebb, but with the advent of an excellent staff nurse and later, a ward sister with paediatric experience, the mortality rate started to fall and a fatal termination no longer appeared inevitable. I have since felt that the greatest single factor in prognosis rests on the standard of nursing available.

The infants were admitted to the mothers-and-babies ward, and, if possible, placed in a corner of the ward, but no other precautions could be taken against light and noise. It was always difficult to get the co-operation of the mothers to leave their babies in the cots and our experiences were very similar to those described by Jelliffe (1950) in Ibadan. All infants were given daily injections of procaine penicillin for five days. The umbilical region was cleaned with a dilute antiseptic, and a dry dressing was applied, but neither local infiltration with A.T.S. nor umbilectomy was used. Umbilectomy was recommended by Vinnard (1945), but an operation of this nature would be abhorrent to the mind of an African native, who always has a high regard for his umbilicus, and would not tolerate its removal.

Sodium phenobarbitone gr. $\frac{1}{8}$-$\frac{1}{4}$ was used as a basal sedative and repeated when necessary in conjunction with intramuscular paraldehyde, but the latter was used as infrequently as possible owing to the danger of tissue necrosis. Chloral hydrate was used as an alternative in a dosage of 1-2 gr. when a change in therapy was indicated. Mephenesin elixir was given a prolonged trial, but the drug was considered of little value in producing muscular relaxation in tetanus neonatorum.

More recently a combination of chlorpromazine 10 mg. given intramuscularly with sodium phenobarbitone became standard treatment and this proved the most promising method of treatment. Injections of chlorpromazine were required on an average every four hours during the first two or three days, but were discontinued as soon as possible as the injections tended to give rise to hard, indurated lumps. Fortunately, these rarely suppurated. Cole and Robertson (1955) described the successful

treatment of a 12-day-old infant in Tanganyika with chlorpromazine and our experience confirmed their observations on its value in controlling spasms, although its effect passes off within a few hours.

Tracheotomy was never performed as there was insufficient trained staff available for adequate supervision after the operation, and the dangers of tracheotomy in these conditions were considered to outweigh the likelihood of a favourable result.

Sickle Cell Disease. There is still no known cure for this disease, and blood transfusion is still the most valuable form of therapy to counteract the acute anaemia which develops during a sickle cell crisis. Hopes were raised when Hilkovitz (1957) reported that acetazolamide had reduced the degree of sickling in a child suffering from sickle cell disease, and it was given an immediate trial in Sierra Leone. The news that there was a new drug for this incapacitating disease soon percolated to the African population and within a few weeks the pharmacies in Freetown had no supplies left and the 'black-market' price bounded to five times that of the official price list.

Unfortunately results did not come up to expectations. In those patients who were admitted in the throes of an attack, the drug was given in full dosage as recommended by Hilkovitz and sometimes it was increased still further, but it never appeared to reduce the length or severity of an attack. In the case of the boy already mentioned whose attacks commenced with pain in the sternum, acetazolamide was given to the mother to administer as soon as an attack appeared to be developing, but this failed to alter the pattern of his attacks. It was clearly too expensive a drug for the average patient to receive prophylactically, but even this method was tried on several patients who suffered from frequent crises, but to no avail. Disappointing results have also been recorded by Macdougall and Jacob (1959) and dos Santos and Lehmann (1959).

Comments

Many of the common diseases of childhood that occur in the United Kingdom were to be seen in Sierra Leone, and the practice of paediatrics in Freetown was not confined to tropical diseases alone. However, even among diseases common to both temperate and tropical climates, there was a great difference in prognosis. The background of malnutrition in its various forms pervaded through all illnesses and, in general, children showed a lack of resilience and an inability to combat serious infection. Most children had no spare flesh upon which to draw when they contracted such debilitating ailments as the common infectious diseases of childhood, and were readily susceptible to secondary infections. Cancrum oris was seen on several occasions, and in the present series two of the four children who developed eye complications during an attack of measles became totally blind.

Certain conditions commonly seen in the United Kingdom were rare, notably the allergic disorders. Asthma was only seen occasionally, but the attacks proved difficult to control. I have never seen infantile eczema in an African in either Kenya or Sierra Leone. My attention was focused on this latter condition in 1958 when I visited the Belgrave Hospital for Children, London, at the invitation of Dr. R. B. Martin, and saw in one session about a dozen infants and children of West Indian extraction with infantile eczema. The other striking feature was their excellent physical development in contrast with that of the children I was accustomed to see in Freetown.

Toxoplasmosis in its acute form in infancy or early childhood was never recognized, and yet I saw over 30 patients with this disease presenting with choroido-retinitis in varying degrees of activity or quiescence during four years in Freetown. The youngest patient was a girl of 12 years and about half of them were still at school or college. The patients invariably complained of some degree of deterioration of vision, and as a number of them were studying for examinations, they usually visited one of the opticians in Freetown with a request for glasses to assist them in reading. A few patients complained of a mild degree of frontal headache such as might occur with eye-strain in addition to impaired vision, but apart from this, toxoplasmosis appeared to be symptomless and more than half the patients were referred to me by opticians.

Treatment employed in treating toxoplasmosis was confined to the use of pyrimethamine (tabs. once or twice daily according to the weight of the patient) for a minimum of three months. In those patients with a recent history of blurring of vision and showing acute choroidoretinitis, improvement was usually noticed between three to six weeks of commencing treatment, but no improvement was seen when the symptoms had been present for six months or longer. The only toxic sign seen after the use of such a large dosage of pyrimethamine was an increase in depth of pigmentation, particularly in the palmar creases of the hands, which, although normally almost free from pigmentation, after three months' therapy were often almost jet-black.

Summary and Conclusions

An account is given of paediatric experience gained during four years in Freetown, Sierra Leone,

with an analysis of 422 infants and children who were admitted to the children's medical ward during the last six-month period.

Parental ignorance, fear, and superstition were partly responsible for the high mortality rate in infancy and early childhood. Many children were brought to hospital in a moribund condition, suffering from illnesses which could have been cured if they had been brought earlier. The high incidence of tetanus neonatorum is an example of the degree of ignorance and lack of hygiene to be found among the general population; a lowering of the mortality rate in childhood generally is not likely to be appreciable until education in public health measures becomes effective.

The presence of malnutrition among children was a major factor in the high morbidity and mortality rates, and was due to a combination of poverty and ignorance in dietary matters.

I am indebted to Dr. T. P. Eddy, late Director of Medical Services, Sierra Leone, and to his successor, Dr. H. M. S. Boardman, for their encouragement in the writing of this paper.

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THE EFFECT OF TROPICAL AND OTHER ENVIRONMENTAL FACTORS ON STATURE AND SUBCUTANEOUS FAT IN KAMPALA NURSERY SCHOOL CHILDREN

BY

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The adaptation of European children to life in tropical climates is a subject fraught with emotional and political undercurrents. The literature on the subject can be divided into two main groups: that concerning children living in areas where the European immigrant population is becoming assured, such as tropical Australia and Central America where the favourable aspects are emphasized (Cilento, 1925; Grenfell Price, 1935) and Colonial areas such as East Africa where the position is less secure and reports express anxiety (Mackinnon, 1923; De Boer, 1924; Roberts, 1949). The 'lassitude and mental dulness' of European school children in Kenya described in the very early papers is still discussed, although lassitude among children in those days could almost certainly have been attributed to malaria and other parasitic diseases which were far more prevalent then than now. All the authors quoted found that tropical European school children were taller at all ages than children in England and that the onset of the puberty growth spurt was earlier, especially in girls. The reaction to this feature was one of approval on the part of the Australian authors and of anxiety ('depressing effects of a hot house atmosphere') on the part of the East African authors.

This paper is concerned, not with older children around whom an emotional rearguard action is still being fought, but with children of nursery school age (4 to 5½ years) in Kampala. Parents of these children were circularized and interviewed to find out whether they wished to bring any special complaints regarding their children to the notice of the school doctor. Almost all expressed some form of anxiety as to the suitability of the climate to their children's health. Many complained that their children had no appetite in Kampala although they ate satisfactorily while on leave in Great Britain. It occurred to me that this may have been a normal reaction to climate and that in a tropical climate one might expect to feel more comfortable with a thinner layer of subcutaneous fat. Very little work has been done on this aspect of adjustment to climate, although there is some evidence that body weight and basal metabolism tend to be lower in hot climates (Roberts, 1953).

An attempt was therefore made to compare the height, weight and amount of subcutaneous fat (based on arm measurements and skin fold using a Harpenden caliper) of European children aged 4-5½ years in Kampala with children of the same age in England (Acheson, Kemp and Parfit, 1955; Hammond, 1955) and with Kampala African children of the same ages.

Method

Height, weight, upper arm length, mid-arm circumference and triceps skinfold thickness were recorded for each child using a method which has been described in another paper (McFie and Welbourn, 1960). This method differed from that usually followed because the measurements were taken with the arm flexed to a right angle. This gave arm circumference readings about 2-5 mm. higher than those taken with the arm extended. Because of this difference in method the arm circumference readings were not included in this report. The skinfold measurements were taken with the muscle freely mobile under the fat and the arm relaxed, and in these conditions there was no difference between the readings in extension and right-angle flexion.

The Children and their Environment

The European children, all from Great Britain, were resident in Kampala for periods ranging from 21-40 months, spending three to 10 months on leave in the United Kingdom at the end of each period in Kampala. Their parents were in either pro-

fessional or skilled occupations. For purposes of comparison the heights of children in the Oxford Survey (Acheson *et al.*, 1955) were used. The children in the Oxford Survey were also of superior social class (only 16% were in classes IV and V) and thus, although the Kampala families probably had a slightly higher standard of living than those in Oxford, the two groups were comparable.

The African children were all of the highest socio-economic class. They were attending an expensive private nursery school and their parents were all in professional employment. In spite of this, their standard of living was on the whole not so high as that of the European children and although all the children were having milk daily, a varied diet and regular meals, their diet was still for traditional reasons a little overbalanced in favour of carbohydrate. None of the children had enlarged spleens, and none were suffering from the effects of tropical parasitic diseases. They were all of the same tribe (Ganda).

The climate of Kampala is not extremely tropical. Indoor temperatures range from 75 to 80° F. throughout the year; rainfall is moderate and evenly distributed through the year. The countryside is always green and there are no seasonal changes. The altitude is 3,700 ft. above sea level. European children run about everywhere in the sun without hats; they get far hotter than their parents and seem to enjoy it. Their parents often hanker after sharp air and bracing winds, and when this is so they are inclined to worry about the possible ill effects of a tropical climate.

Results

Heights and Weights. Fig. 1 shows the distribution of heights and weights of European and African children in Kampala compared with heights and weights of children in the Oxford Survey. Since all the children in the present series were weighed at different ages, no attempt was made to calculate average weights at different ages. Instead, individual readings of weight and height for age were plotted in relation to mean heights and weights of children in the Oxford Survey: the Oxford Survey weights and heights for age were plotted showing the mean (M) and the values of one, two and three standard deviations above (+1, +2 and +3) and below (−1, −2 and −3) the mean. Individual readings in the present series were plotted on this graph and the number of readings in relation to the mean were counted as follows: Above the mean; M to +1 s.d.; +1 s.d. to +2 s.d.; +2 s.d. to +3 s.d.: and below the mean: M to −1 s.d.; −1 s.d. to −2 s.d.; −2 s.d. to −3 s.d. The numbers of readings in each group are shown as histograms in Fig. 1.

Comparing Kampala European children with children in the Oxford Survey, the weights of the children of both sexes and the heights of the girls were similar in Kampala and Oxford (Fig. 1). There was a slight superiority in height of the Kampala European boys over the Oxford boys which was only just significant and represented a difference in mean height about 0·5 in. (1·3 cm.). Comparing the Kampala European with Kampala African, there was a marked superiority in both height and weight of the European children of both sexes, representing a difference in mean height of about 1·25 in. (3·2 cm.).

Arm Length. Arm length ranged from 193 mm. at 4 years to 208 mm. at 5 years. There was no difference between African and European children or between the sexes.

Subcutaneous Fat. The Table shows the average triceps skinfold readings of Kampala African and European children compared with children in England measured by Hammond (1955). Comparing Kampala European children with children in England, the readings for the girls in England and Kampala were similar, but the boys in Kampala had slightly (just significantly) less subcutaneous fat than boys in London. The readings for the Kampala African children of both sexes were 0·5 mm. lower than the Kampala European children.

Discussion

In a study of pre-school age children in Durban, Phillips (1953) emphasized that the economic group to which a child belonged was far more important in determining the stature of the child than the ethnic group. In another study in Durban, Lewis (1959) emphasized the importance of social and cultural factors influencing the health of children of this age. Phillips (1953) found that the heights and weights of European pre-school age children in Durban were similar to those of European children of the same income groups in other parts of the world, though his upper-income group children were slightly taller and heavier than upper-income group children in sources quoted by Phillips and also than European children in the present series.

In neither of the above studies was the question of adaptation to climate discussed, although Phillips noted that there was no difference in stature between lower income group children in Johannesburg, Melbourne and London. In the present

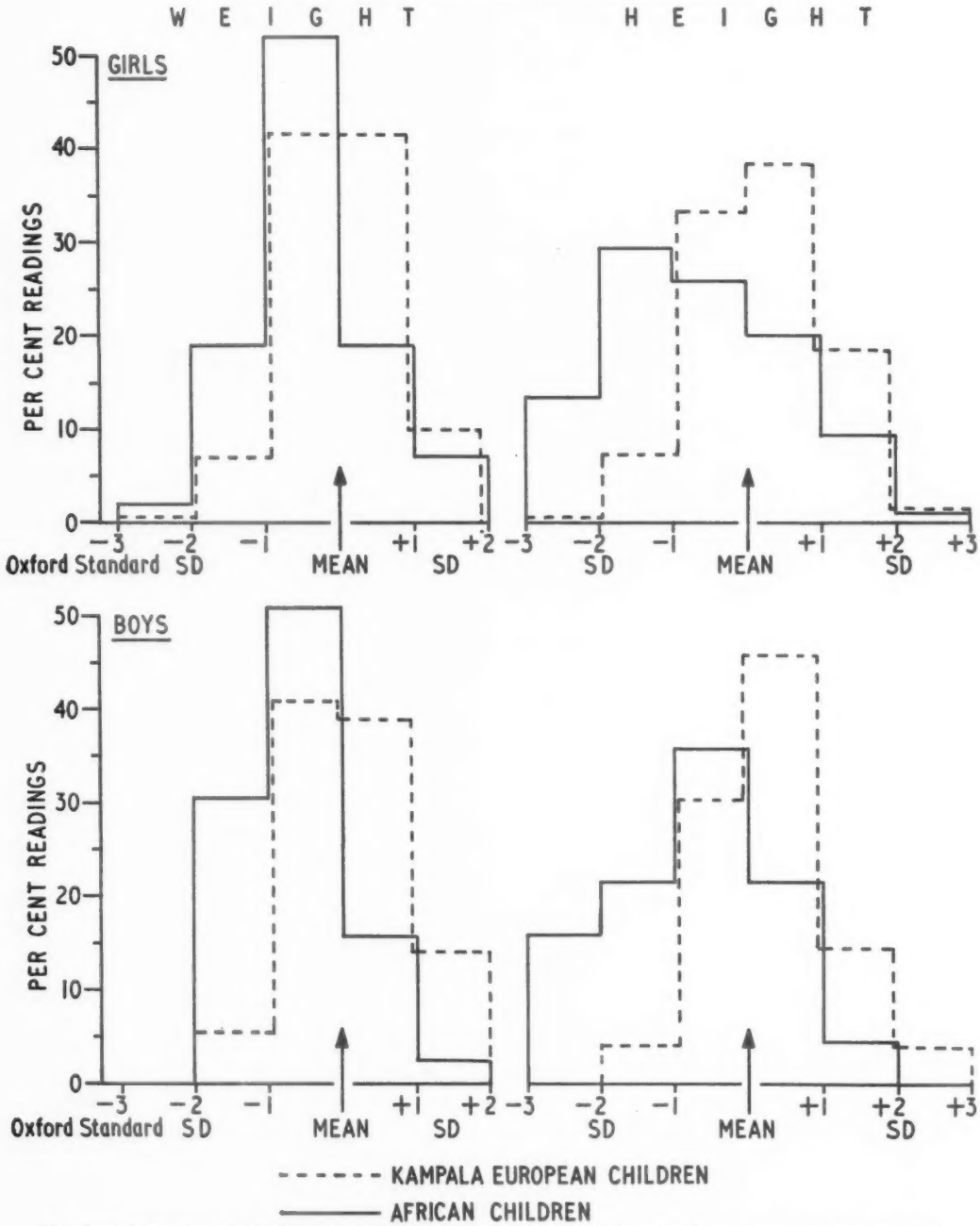


FIG. 1.—Distribution of heights and weights of European and African children in Kampala with Oxford Standard.

series the heights, weights and skinfold measurements of European children in Kampala were practically similar to those of children in England. The Kampala European boys were slightly taller and had slightly less subcutaneous fat than children in England, but these differences were only just significant and probably not important. The lack of appetite and failure to grow well reported by parents of Kampala European children were undoubtedly subjective impressions based on the parents' attitude to conditions of living in Kampala. No objective evidence was found either of the ill effects of a tropical environment or of possible beneficial adaptations to the environment on the part of the children.

It has already been shown (Welbourn, 1955) that

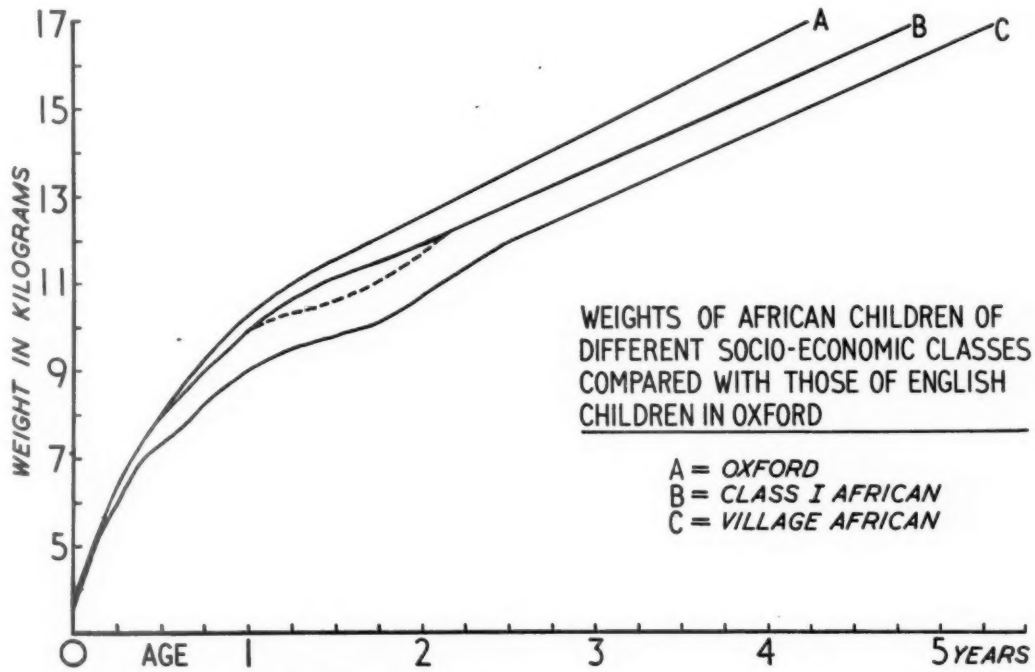
TABLE

SKINFOLD THICKNESSES OF AFRICAN AND EUROPEAN CHILDREN IN KAMPALA COMPARED WITH CHILDREN IN ENGLAND

	Kampala African		Kampala European		England (Hammond)			
					Boys		Girls	
	Boys	Girls	Boys	Girls	4–5 yrs	5–6 yrs	4–5 yrs	5–6 yrs
Total children measured	82	78	101	100	43	49	44	45
Average skinfold thickness (mm.)	7·3	8·0	8·8	9·5	9·34	9·13	10·24	9·42
Standard deviation	1·50	1·75	1·42	1·85				

the increase in weight and height of Uganda African infants and pre-school children is poor compared with children in Western countries, and that this difference is less marked among children of highly educated families. This is well illustrated in Fig. 2 which shows increase in weight from birth to 6 years of African boys of different socio-economic groups compared with boys of the same ages in England. Weight curves for girls have not been shown; except that the girls were a little lighter, the curves for the girls were exactly similar to those for boys shown in Fig. 2. The curve for 'class 1' African children was derived from figures published by Jelliffe and Dean (1959) together with weights of children attending child welfare clinics and nursery schools.

The weight curve of these children was above that for children of the same tribe of lower socio-economic groups attending ordinary village child welfare clinics: the difference first became apparent at 3 to 6 months, and thereafter there was a difference of about 2 to 3·5 lb. (0·9 to 1·6 kg.). The difference was most marked during the 18- to 30-month age period, because during this time Uganda African children suffered most severely from malnutrition, infections and traumatic experiences associated with



G. 2.—Weights of African boys of different socio-economic classes compared with those of English children in Oxford Survey.

= Oxford Survey.
= Class 1 African standard curve. True curve shown by dotted line.
= Village African.

weaning and maternal separation (Geber and Dean, 1957; Welbourn, 1959). Even the 'class 1' African children gained weight less well in this age period: the true weight curve showed a dip maximal at 0·5 kg. below the standard curve at 20 months (Burgess, 1960), which was not shown on the standard figures (Jelliffe and Dean, 1959). This dip showed that even the children in 'class 1' were underfed, probably because for cultural reasons they were offered food less frequently and regularly than children in England, and the main meal of the day was likely to be overbalanced in favour of bulky carbohydrate.

The nursery schoolchildren in the present series were shorter, lighter, had less subcutaneous fat and lower muscle estimate values than English children of the same ages in Kampala. It cannot be known with certainty how far these differences were attributable to ethnic characteristics. Neither is it certain whether lack of subcutaneous fat is advantageous in a tropical climate. Certainly many of the African nursery schoolchildren gave an impression of toughness and wiriness, and it is common experience in inter-racial children's sports in Kampala that wiry little African and Asian children usually have the advantage over their heavier European contemporaries. Although the African nursery schoolchildren were from the best possible socio-economic group, their standard of living was still not as high as that of European children in Kampala. Socio-economic and cultural factors which had affected the child throughout life and particularly during the period after weaning were probably more important than ethnic or climatic factors in determining the differences observed between European and African children in Kampala.

Summary

Heights, weights, upper-arm length, circumferences and skinfold were measured in European and African children aged from 4 to 5½ years attending Kampala nursery schools. Measurements of Kampala European children were found to be almost the same as those of children in England. The African children were shorter, lighter and had less subcutaneous fat than the European children. The arm lengths of the two groups were similar.

It was suggested that the growth of the Kampala European children was satisfactory and that the differences between the European and African children were due more to socio-economic and cultural than to climatic factors.

I wish to record my thanks to Dr. C. P. Welter and Mr. Paul Mogambi of the Department of Mathematics, Makerere University College, Kampala, for their help with the compilation of statistics and for preparing the histograms shown in Fig. 1.

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THE INFLUENCE OF MATERNAL IRON-DEFICIENCY ANAEMIA ON THE HAEMOGLOBIN OF THE INFANT

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The object of this study is to define the part played by maternal iron-deficiency anaemia in the pathogenesis of iron deficiency anaemia in infancy, a condition commonly found in Cape Town (Lanzkowsky and McKenzie, 1959; Lanzkowsky, 1959 and 1960a).

A number of early reports on the effect of maternal iron-deficiency anaemia on the newborn have indicated that maternal anaemia does not cause anaemia in the infant soon after birth and that the foetus avails itself of maternal blood-forming materials necessary for its own requirement irrespective of the condition of maternal blood (Baar and Stransky, 1928; Strauss, 1933; Strauss and Castle, 1933; Fullerton, 1937; Davidson and Fullerton, 1938). This view has been opposed by Maurer, Greengard and Kluver (1932). Paradoxically, Strean and Gottlieb (1936) found that the greater the maternal anaemia, the greater the foetal polycythaemia.

More recently Sisson and Lund (1958), basing the diagnosis of iron-deficiency anaemia on calculation of maternal and infant red cell volume and haemoglobin mass, concluded that infants of anaemic mothers frequently did have an iron-deficiency anaemia. Woodruff and Bridgeforth (1953) and Sturgeon (1959), on the other hand, are at variance with the work of Sisson and Lund and have convincingly shown in large and well-controlled series that there is no difference in the state of iron nutrition in groups of infants born to mothers with various degrees of iron nutrition.

Many authors have endorsed the statement that infants born to anaemic mothers become anaemic towards the end of the first year, although scientific evidence supporting this concept is very scanty. Macaulay (1931), Abt and Nagel (1932), Neale and Haworsley (1933), Parsons (1933), Strauss (1933, 1935) and Hahn, Carothers, Darby, Martin, Shepard, Cannon, Beam, Densen, Peterson and McClellan (1951) all favoured the view that maternal iron deficiency was a factor in the pathogenesis of iron-deficiency anaemia in infants during the first year of life due to deficient iron storage in the foetal liver. Most of these early reports are unsatisfactory for various reasons. Strauss (1933, 1935) has been widely quoted in support of the contention that maternal iron deficiency causes a reduction of the haemoglobin blood level in the infant during the latter half of the first year of life, but his investigation did not take into account such pertinent factors as birth weight, rate of growth, type of feeding and incidence of infection. In other similar reports the clinical data presented do not bear critical analysis, because control series were not undertaken and the evidence presented in favour of such a hypothesis does not appear to justify the conclusions drawn therefrom.

Fullerton (1937) alone of the earlier investigators did not accept the view that there was a relationship between maternal anaemia and anaemia in the baby during the latter half of the first year of its life. He followed a large number of cases, with a control series, over a long period and took into account such relevant details as birth weight and method of feeding. This earlier work has been verified more recently by Woodruff and Bridgeforth (1953) and Sturgeon (1959) who have shown that the state of an infant's iron nutrition at 1 year of age is not influenced by the level of maternal iron nutrition during pregnancy.

In any assessment of maternal influence on the iron nutrition of the infant it is essential to distinguish clearly between the nutritional state of the infant at birth and at a later stage of its development. If the recent view is accepted that at birth there is no substantial store of iron in any of the infant's tissues except in the circulating haemoglobin, it is apparent that after some months of extra-uterine life the dietary iron intake may have influenced the haemoglobin level.

Most of the literature on the relationship between

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maternal and infant haemoglobin levels is confused and difficult to assess because the fundamentally important *time factor* had not been taken into account. The present study was undertaken to investigate the effect of maternal iron-deficiency anaemia on the haemoglobin of the infant during the first three months of life. This investigation consists of two parts: The first deals with the effect of maternal iron-deficiency anaemia at term on the haemoglobin level of the infant in the first 24 hours of life, and the second part with the effect of maternal iron-deficiency anaemia at term on the haemoglobin levels in these infants at 3 months of age, i.e. before dietary effects are likely to have exerted any material influence on the infants' iron nutrition.

Present Investigation

The Newborn Infant. Fifty-nine mothers and their newborn infants were investigated. These mothers were drawn from a random selection of women attending antenatal clinics and were confined at various maternity institutions attached to the University of Cape Town. All these women were given a general medical examination at their first attendance and were found to be healthy. Serological tests for syphilis were negative in all cases. Only those who had full-term normal pregnancies and a normal labour and who had been delivered without untoward incident were included in this series. Women with a history of haemorrhage before, after or during delivery or whose delivery was in any way abnormal, were excluded from this investigation. None had received prophylactic iron therapy during pregnancy.

The mean income per week of the families from which these women came was £14·09 and £5·27 for White and Cape Coloured women respectively. According to the criteria adopted by Bronte-Stewart, Keys, Brock, Moodie, Keys and Antonis (1955) and Moodie (1959) these amounts place these women in the 'medium income' groups of their respective sections in the community.

Fifty-nine cases were selected from this random sample designed to provide two groups, one comprising women who were severely anaemic at term and the other women who were not anaemic at term. It was hoped that such a division based on the presence or absence of severe iron-deficiency anaemia would yield clear-cut results.

The diagnosis of maternal iron-deficiency anaemia was made on the basis of mean corpuscular haemoglobin concentration (M.C.H.C.) values. Most investigators in this field have diagnosed maternal iron-deficiency anaemia solely on the basis of a low haemoglobin level; the fallacy of using such a criterion for the diagnosis of anaemia especially in pregnant women is well recognized.

The 59 cases were divided into two groups.

Group A: 33 women (18 White, 15 Cape Coloured) all with M.C.H.C. levels of 27% or less;

Group B: 26 women (11 White, 15 Cape Coloured) all with M.C.H.C. levels of 31% or more.

The difference in the average mean corpuscular haemoglobin concentration levels in the two groups of mothers was highly significant statistically.

The slight difference between the mean birth weights of the infants born to mothers in group A and the infants of the mothers in group B was not statistically significant.

In the total series of 29 White babies in both groups there were 12 cases (eight in group A and four in group B) in which the umbilical cord had been clamped immediately after birth and 17 (10 in group A and seven in group B) in which the cords were stripped and clamped later. The results in so far as they concerned the infants were analysed separately, because of the variation in haemoglobin levels that occur when umbilical cords are clamped at different times after birth (Lanzkowsky, 1960b). This variability amongst the White infants was taken into account in analysing the results and the White infants therefore were considered under two sub-groups for both group A and group B. The method of cord management was the same in all 30 Cape Coloured infants; the results in these infants were therefore analysed simply on the basis of whether they belonged to either group A or group B. How these cases were divided and the number of cases in each group and sub-group is shown below in simplified form.

59 parturient women
- 33 group A (low M.C.H.C.)
  - 8 White, early clamped
  - 10 White, late clamped
  - 15 Cape Coloured
- 26 group B (high M.C.H.C.)
  - 4 White, early clamped
  - 7 White, late clamped
  - 15 Cape Coloured

METHODS. Blood investigations were done on venous blood in mothers and on capillary blood in infants. The haemoglobin estimations were carried out by the oxyhaemoglobin method with a Klett-Summerson colorimeter previously calibrated against standard haemin and cyanmethaemoglobin solutions. Packed cell volume estimations were made in accordance with the standard Wintrobe procedure (Wintrobe, 1929).

TABLE

COMPARISON OF MEAN WEIGHTS AND HAEMOGLOBIN LEVELS IN FIRST 24 HOURS OF LIFE AND AT 3 MONTHS OF AGE IN INFANTS BORN TO MOTHERS IN GROUP A WITH INFANTS BORN TO MOTHERS IN GROUP B

Race and Mode of Cord Clamping	Groups	Mean Maternal M.C.H.C. %	First 24 hours of Life			At 3 Months of Age		
			No. of Cases	Mean Birth Weight (lb.)	Mean Hb g. %	Mean Hb g. %	Mean Weight (lb.)	No. of Cases
White (early clamped) ..	A	26·63	8	7·55	19·04	11·42	11·55	6
	B	31·68	4	7·60	20·30	11·93	12·87	3
	Significance	p<0·001	—	p>0·25	p>0·25	p>0·25	p>0·25	—
White (late clamped) ..	A	25·06	10	7·57	18·70	10·85	11·23	8
	B	32·04	7	6·87	19·47	11·07	11·34	7
	Significance	p<0·001	—	p>0·10	p>0·25	p>0·25	p>0·25	—
Cape Coloured	A	26·01	15	6·88	18·99	10·65	10·95	13
	B	32·49	15	7·08	18·90	11·44	12·00	11
	Significance	p<0·001	—	p>0·25	p>0·25	p>0·10	p>0·10	—

RESULTS. The Table shows that the mean haemoglobin levels in the first 24 hours of life in infants born to mothers in group A were 19·04, 18·70 and 18·99 g. % for the White early-clamped, White late-clamped and Cape Coloured infants respectively, as compared with values of 20·30, 19·47 and 18·90 g. % obtained from the corresponding sub-groups of infants born to mothers in group B. The difference in haemoglobin values between the corresponding sub-groups of infants born to mothers in group A and in group B was not statistically significant.

The Infant at the Age of 3 Months. The investigation outlined above was continued until the infants were 3 months old. A number of variables, such as body weight, diet and infections, had to be considered in making deductions from observations. Were such an investigation to be continued beyond the third month of the infant's life, it would not be possible to interpret the significance of the results thereof accurately.

MATERIAL. The 59 infants of the mothers comprising group A and group B described earlier in this paper, were kept under observation until they were 3 months old. None received prophylactic iron medication during this time. Eleven mothers failed to bring their infants back for a final blood examination and this part of the investigation is therefore based on a total of 48 infants. None of these had suffered from any illness since birth. The two groups of infants were similar as regards birth weight and body weight at 3 months of age. The Table shows that the White early-clamped group A infants and the White late-clamped group A and group B infants (totalling 21 out of 24 White infants) had similar mean weights. The slightly higher mean weight of the three White early-clamped infants in group B is not of sufficient significance to disturb the homogeneity of the group.

RESULTS. The Table shows that the mean haemoglobin levels at 3 months of age were 11·42 g. %, 10·85 g. % and 10·65 g. % for the White early-clamped, White late-clamped and Cape Coloured infants respectively born to mothers in group A, as compared with values of 11·93 g. %, 11·07 g. % and 11·44 g. % in the corresponding sub-groups of infants born to mothers in group B. These differences are not statistically significant. The fall in haemoglobin level between birth and 3 months of age was approximately 8 g. % in all infants. Such a fall is normally to be expected (Lanzkowsky, 1959 and 1960a).

If more evidence were required it could doubtless be obtained by the examination of haemoglobin levels in infants born to extremely anaemic mothers. A case of such severity was seen after the conclusion of this investigation. The maternal haemoglobin was 4·5 g. % at six weeks before term and fell to 2 g. % at the time of delivery. This mother had all the manifestations of an iron-deficiency anaemia. The haemoglobin level of her infant when first recorded at 3 weeks of age was 15·5 g. % and at 3 months of age, it had fallen to 11 g. %.

Discussion

The theoretical explanation usually given for the pathogenesis of anaemia in infants born to iron-deficient mothers is that their hepatic store of iron is inadequate and that early exhaustion of that store occurs during the milk-feeding period of early infancy (Mackay, 1931; Neale and Hawksley, 1933; Strauss, 1933).

The above postulate has been tested experimentally in animals. Happ (1922) and Mitchell and Vaughn (1927) showed that when rats were fed on a diet low in iron, anaemia occurred in the second and third generations of their offspring. Similar observations have been reported for mice (Schmidt-Marburg, 1912) and for pigs (McGowan and Crichton, 1924). Alt (1938), experimenting on rats, studied the offspring of female rats made anaemic by low iron diets. He showed that a single pregnancy in these female rats caused a decrease in the iron store in the liver without affecting the haemoglobin content of the blood. A second pregnancy, however, resulted in moderate anaemia due to iron deficiency. First litter offspring of these female rats with mild iron deficiency had normal haemoglobin values at birth, but they had a considerable reduction in their iron store. Second litter offspring of the female rats who were more iron deficient showed a decrease in haemoglobin content at birth and a reduction of the total iron content of these new-born rats to one-fourth of normal. Alt's work demonstrated that reduction of foetal liver iron store preceded the development of anaemia.

It is unsound to presume an analogy between anaemia in infants and in animals without considering the fundamental differences which exist between the iron metabolism of experimental animals and of humans (Fullerton, 1937). Rabbits increase their weight six-fold during the almost exclusive period of milk-feeding during the first four weeks of life, and rats grow even more rapidly. A normal human infant gains approximately one-sixth of its birth weight in that time and it is obvious that its iron requirement is relatively much less than that of the rabbit or the rat. The liver store of iron at birth is not comparable in humans and animals. Moreover, the ratio of total foetal weight to maternal weight is much higher in experimental animals than in humans. For example, a female rat weighing 250 g. has an average litter of eight or nine young with a total weight of 36 to 45 g., giving a foetal to maternal ratio of about 1 in 6, whereas the human ratio is much less, approximately 1 in 16. In the rat it is far more likely than in human beings that maternal iron deficiency will result in foetal iron deficiency. Inferences to be drawn from animal experimental investigation cannot be applied unreservedly, if at all, to man.

The iron store in the livers of human newborns was estimated by Gladstone (1932), Sheldon (1932) and Toverud (1935). They found an average of approximately 32, 50 and 60 mg. respectively. In such investigations failure to obtain livers in a blood-free state (presumably an impossibility) vitiates the results, especially if current opinion is correct in maintaining that the circulating haemoglobin carries most of the baby's supply of iron. Fullerton (1937), working on the assumption that there is no iron reserve in the liver at birth, calculated that a hypothetical deficit of 50 mg. of liver iron at birth would only reduce the blood iron from an estimated 333 mg. to 283 mg. by the time the infant reached the age of 9 months, and this would give a haemoglobin level of 73%. If this is correct, a partial deficiency in the liver iron store at birth could have only a slight effect on the haemoglobin level in later infancy.

Smith, Rosello, Say and Yeya (1955), having given transfusions of erythrocytes tagged with Fe^{55} to mothers, judged that transplacentally acquired iron, not present in haemoglobin at the time of birth, was meagre in relation to the amounts of iron contained in circulating haemoglobin. The view that the blood of the newborn baby is the major source of the iron to be used later in maintaining haemoglobin levels is well documented (Lintzel, Rechenberger and Schairer, 1944; Hemmeler, 1946; Neander and Vahlquist, 1949; Langley, 1951; McCance and Widdowson, 1951; Josephs, 1953).

Smith *et al.* (1955) also showed that transplacental Fe^{55} was 'diluted' by dietary iron when the infants were 3 to 4 months old. They showed that between the third or fourth month and the second year of age the haemoglobin level increased only slightly, while the total amount of haemoglobin was doubled, primarily by the addition of haemoglobin derived from dietary iron. This indicates that the older the infant, the less the importance of transplacental iron as compared with dietary iron. Even if at birth there should be a deficiency in total body iron associated with frank maternal iron-deficiency anaemia, this can be compensated for at 1 year of age by the iron in the infants' diet.

There is no reliable evidence to support the contention that a close relationship exists between maternal haemoglobin levels and those in the infant at any age after birth in human beings. The present work is in agreement with that of Woodruff and Bridgeforth (1953) and Sturgeon (1959) who have shown that the two levels are not interdependent at birth. The available evidence supporting the presence of a substantial store of iron in the liver is not convincing.

The work done by Sturgeon and the results of the present investigation do not support the concept that maternal iron deficiency has any effect whatsoever on the haemoglobin level of the baby at 3 months of age in infants of normal birth weight

who have remained well since birth. It certainly seems that, so far as normal infants are concerned, they are parasitic on maternal iron and look after their own well-being in this respect very efficiently while *in utero*. Contrary views appear to have been based on observations which have ignored certain essentials. A careful attempt was made to control these factors in the present investigation. Many of the earlier workers cannot be blamed for not having taken such factors into consideration. The advancement of knowledge and development of interest in research has thrown into prominence many facets in this regard which were previously considered to be of little importance.

Summary

A review of the literature indicates that there is controversy as to whether maternal iron-deficiency anaemia influences the level of haemoglobin in the blood of infants or not. The present survey was designed to investigate this problem.

The possible influence of maternal iron-deficiency anaemia on the infant was considered under two headings: (*a*) in the newborn infant and (*b*) at 3 months of age, before dietary effects are likely to have influenced the infant's iron nutrition.

Selected mothers (White and Cape Coloured) were divided into two groups: one consisting of women whose mean corpuscular haemoglobin concentration values were 27% or less at term and the other, whose values were 31% or more. The infants of these mothers were investigated.

It was found that there was no significant difference of mean haemoglobin level in the infants, during the first 24 hours of life or at 3 months of age, born to either the anaemic or non-anaemic mothers.

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CONGENITAL THROMBOCYTOPENIC PURPURA TREATED BY EXCHANGE TRANSFUSION

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The occurrence of thrombocytopenic purpura in babies born to mothers with idiopathic thrombocytopenia is a well recognized though uncommon clinical entity. Robson and Walker (1951) were able to collect from the literature only 19 definite and nine probable examples of this association.

The suggestion of Epstein, Lozner, Cobbey and Davidson (1950) that this type of congenital thrombocytopenic purpura results from the transfer across the placenta of a maternal factor capable of causing thrombocytopenia has recently received support with the demonstration of platelet agglutinins in the serum of both mother and child (Harrington, Sprague, Minnich, Moore, Aulvin and Dubach, 1953; Vanderbroucke and Verstraete, 1955; Tullis, 1956; Schoen, King and Duane, 1956). In view of these findings it might be expected that exchange transfusion of affected infants would, by removing the acquired platelet antibodies, shorten the period of thrombocytopenia and so lessen the risk of haemorrhage and death. We report below observations on a baby with congenital thrombocytopenic purpura who was treated in this manner.

Case Report

C.B., now aged 30, had a splenectomy performed when 10 years old for a persistent haemorrhagic disorder regarded as idiopathic thrombocytopenic purpura. Since that time she has had no episodes of excessive bleeding and additionally has had many teeth extracted without trouble.

In June 1958, after an uneventful antenatal period and confinement she was delivered of a female child weighing 6 lb. 3 oz. Shortly after birth the baby was noticed to have purpura which became more widespread during the 14 hours of its survival. Necropsy revealed no haemorrhages other than those in skin; an extensive pneumonia was present and thought to have been the cause of death.

The mother's blood was examined postnatally (August 1958) with the following results: Hb 13·3 g./100 ml., packed cell volume 43%, white cell count 7,100/c.mm., platelets 124,000/c.mm., bleeding time 7 min., clotting time 4 min. 45 sec. (ordinary glass), 6 min. (silicone glass), clot retraction normal in one hour, plasma prothrombin 11 sec. = 100% (control 11 sec. = 100%), fibrinogen 137 mg. % and thromboplastin generation normal. The platelet count was done by the direct method using Rees Ecker diluting fluid on a venous sample of blood, as were all platelet counts on the mother; the normal values for the platelet count as done by this method, are taken as 200-400,000/c.mm.

Her blood was next examined in July 1959, at which time she was six months pregnant. On that occasion the platelets numbered 196,000/c.mm.; all the other previous blood tests were repeated and found to be within normal limits. On October 7, when 39 weeks pregnant, her platelet count was only 84,000/c.mm.; as before, all the other blood tests showed no abnormality. Although thrombocytopenic there was no clinical evidence of any bleeding tendency. On October 22, after an uneventful pregnancy and confinement, she was delivered of a male child weighing 7 lb. 11 oz. The puerperium was uneventful. On the third postnatal day the mother's platelet count was 120,000/c.mm.; three months later it was 128,000/c.mm.

The baby, when examined shortly after birth, was found to have a number of purpuric spots on the face and trunk; no other abnormalities were noted. Examination of blood obtained from the baby when 2 hours old gave the following results: Hb 17·2 g./100 ml., platelets 34,000/c.mm., leucocytes 18,200/c.mm. with a differential white cell count of neutrophils 71%, lymphocytes 27% and monocytes 2%; the bleeding time was 8 min. 30 sec. Examination of a stained film confirmed the lack of platelets: those present showed no morphological abnormality. Blood samples for these and other studies on the baby were obtained by heel prick unless otherwise stated.

When 3 hours old the baby was given an exchange transfusion with 520 ml. 'O' Rhesus negative blood which had been collected during the preceding 24 hours. During the transfusion, which was well tolerated, fresh purpuric spots and ecchymoses appeared mostly on the face. Further fresh crops of purpura were noted during the next three days but not thereafter. Following transfusion he was started on oral cortisone: 25 mg. were given during the next 24 hours followed by 8 mg.

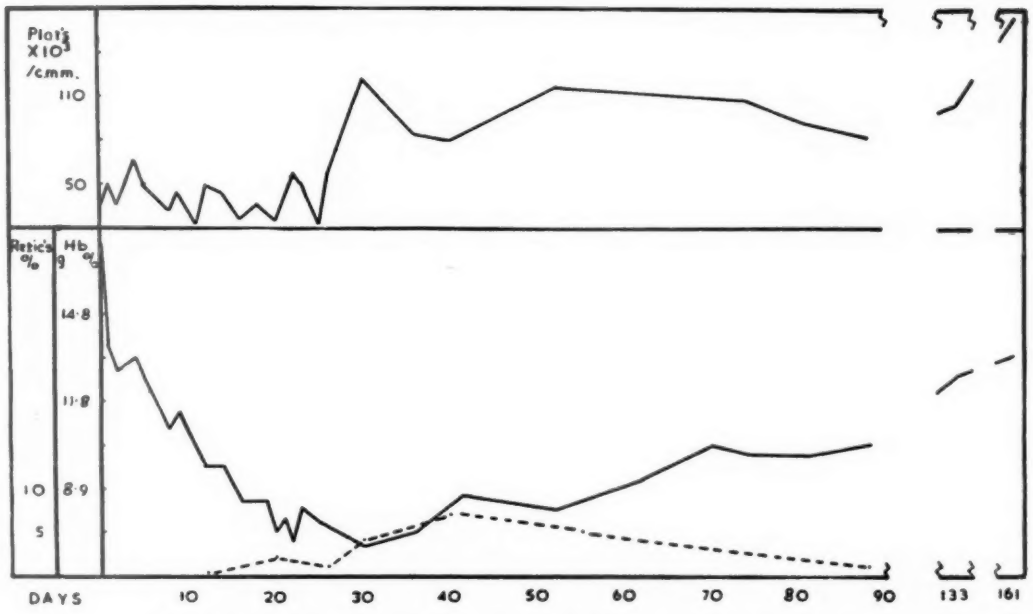

FIG. 1.—Platelet count, haemoglobin level and reticulocyte count during first five months.

daily for four days and 4 mg. daily for five weeks; the dose was then gradually reduced, therapy being discontinued after a further six weeks.

On the day after exchange transfusion the bleeding time had fallen to 6 min. 30 sec., 10 days later it was 5 min. and on all subsequent occasions was less than 4 min. There was, however, no commensurate increase in the platelet count which during the first month never exceeded 80,000/c.mm. Between the first and third months the platelet count varied between 80,000 and 120,000/c.mm. At 4 months the baby's platelet count was still only 106,000/c.mm., but at 5 months this had risen to 166,000 (Fig. 1).

Specimens of venous blood obtained from the baby immediately before and after exchange transfusion and from the mother on the day following delivery were examined for platelet agglutinins by the method described by Kissmeyer-Nielsen (1955). The mother's serum and the baby's pre-transfusion serum both gave a strong positive result whereas the post-transfusion serum from the baby gave only a doubtful positive result. Twenty-six days after birth when the baby's platelet count was still only 59,000/c.mm. both the mother's and baby's sera were again examined for platelet agglutinins. On this occasion the mother's serum gave a strong positive result as previously whereas the baby's was definitely negative.

From a post-transfusion level of 13·7 g./100 ml. the baby's Hb fell steadily to 7·2 g./100 ml. with 1% reticulocytes by the 26th day. Two weeks later the Hb was still only 7·4 g./100 ml. but the reticulocytes had increased to 7%. Thereafter there was a gradual rise in Hb to 13 g./100 ml. at 5 months (Fig. 1).

A sample of bone marrow was aspirated from the iliac crest on the 27th day. Though the sample was diluted with sinusoidal blood the relative number of normoblasts appeared somewhat reduced; otherwise no abnormality was noted and, in particular, appreciable numbers of morphologically normal megakaryocytes were seen.

Except for the development of purpura during the first three days the baby showed no other signs of bleeding. His clinical progress was wholly uneventful, he was bottle-fed throughout and at 3 months weighed 13 lb. 12 oz.

Discussion

It is now established that neonatal thrombocytopenic purpura is a clinical disorder of multiple aetiology (Kaplan, 1959). One form is that which occurs in babies born to mothers suffering from idiopathic thrombocytopenic purpura. Platelet agglutinins have now been demonstrated in both the serum of the mother and of her thrombocytopenic infant on at least five occasions (Harrington *et al.*, 1953; Vanderbroucke and Verstraete, 1955; Tullis, 1956; Schoen *et al.*, 1956, and the present case) thereby providing good reason for believing the disorder to be due to the passive transfer of maternal antibodies.

This type of congenital thrombocytopenic purpura is a self-limiting condition. Complete recovery can be expected provided affected infants survive the hazards of haemorrhage during the early neonatal period. Robson and Walker (1951) and Morris (1954) found that of those infants reported in the literature 15-20% had died within the first

week. The severity of the disease in the mother and the sex of the child are two factors which appear to affect the chances of survival. In general, the more active the disease in the mother the more likely is the baby to be badly affected. There have, however, been reports of affected infants being born to mothers who were either in spontaneous remission or, as in the present case, were clinically well following splenectomy (Robson and Davidson, 1950; Epstein *et al.*, 1950). Secondly, Robson and Walker (1951) in their review of published cases, noted that although slightly more female children were affected all fatalities had occurred in males.

Although fresh purpuric lesions usually cease to appear between the third and 10th day the bleeding time in most cases remains prolonged for some 10 to 28 days. Thrombocytopenia usually persists even longer commonly up to six but rarely beyond 15 weeks with an average duration of the order of 10 weeks (Harrington *et al.*, 1953; Morris, 1954; Vanderbroucke and Verstraete, 1955; Stefanini and Dameshek, 1955).

Only the reports of Schoen *et al.* (1956) and Vanderbroucke and Verstraete (1955) mention the length of time the platelet agglutinins persist in the foetal circulation and only in the latter is this correlated with the platelet count and bleeding time. Schoen *et al.* found platelet agglutinins to be present at 38 but absent at 80 days. Vanderbroucke and Verstraete record a positive result for platelet agglutinins at 39 days with a negative result at 78 days. The platelet count in their patient at these times was 100,000 and 110,000/c.mm.; four weeks later when the baby was 15 weeks old the platelets numbered 260,000/c.mm. The bleeding time which on the first day was 22 min. had fallen to 1½ min. by the 11th day. On the basis of these findings it seems that thrombocytopenia is likely to persist for some time after the disappearance of the platelet agglutinins. This is contrary to the view of Kaplan (1959) who without reference to specific examples records that platelet antibodies may persist after restoration of the platelet count to normal.

In view of the risk to life from haemorrhage during the first week, treatment of these infants must be directed primarily at preventing such catastrophes. No treatment has yet proved effective (Killander, 1959). If one accepts that the thrombocytopenia in the infant is due to the passive transfer of maternal platelet agglutinins then it seems logical to treat these infants by exchange transfusion with the object of washing out the transmitted maternal antibodies. In our patient, no new purpuric lesions appeared after three days, the bleeding time fell to less than 4 min. from the 10th day onwards and the platelet count, initially 34,000/c.mm., remained below 80,000/c.mm. until the 29th day and was still only 166,000/c.mm. at 5 months. Platelet agglutinins present before the start of the exchange transfusion could no longer be identified with certainty immediately after the transfusion and were definitely absent on re-examination of the baby's serum at 26 days. The wide variation in the natural history and the paucity of data relating to the persistence of platelet antibodies make it impossible to assess accurately the value of such therapy by reference to only a single case. Comparison with the reports of Vanderbroucke and Verstraete and Schoen *et al.* suggests that we did succeed in accelerating the elimination of antibodies from the baby's serum. However, there is nothing to indicate that this had any effect in shortening the duration of purpura, prolonged bleeding time and thrombocytopenia. These observations are similar to those of Killander (1959) who alone has treated a similar case by exchange transfusion. In this author's patient bleeding episodes occurred up to 4 weeks and the platelets still numbered only 60,000/c.mm. at 7 weeks.

It is of interest that in both our patient and that of Killander exchange transfusion was followed by a period of anaemia. In the present case there was no evidence to suggest a haemolytic process as the cause of the anaemia; generalized marrow failure can also be excluded as an aetiological factor on the basis of the essentially normal marrow picture. Thus it appears likely that the anaemia was of similar origin to that which not uncommonly occurs after exchange transfusion for haemolytic disease especially when the immediate post-transfusion haemoglobin level is less than 15 g./100 ml. (Gairdner, 1958) as was the case with our patient.

This apparent lack of response to exchange transfusion in congenital thrombocytopenia is in marked contrast to that recorded by Stefanini, Mednicoff and Plitman (1954) on a baby with erythroblastosis foetalis and associated thrombocytopenia. Maternal platelet iso-agglutinins were detected in the baby's serum. After the second of two exchange transfusions performed within 48 hours of birth the purpura disappeared and the platelet count rose promptly from 60,000 to 250,000/c.mm. subsequently remaining above this figure. This type of response is what one might expect if the baby's low platelet count was due solely to the destruction of platelets by circulating antibody. Is the lack of a similar response in babies born to mothers with idiopathic thrombocytopenic purpura indicative of a more complex mechanism? Some support for this view is provided by the observation

that the thrombocytopenia may persist for a considerable time after the disappearance of antibodies (Vanderbroucke and Verstraete, 1955; and the present case).

Corticosteroids are of acknowledged value in the treatment of patients suffering from idiopathic thrombocytopenic purpura and it therefore seems logical to use these drugs on babies with congenital thrombocytopenic purpura. As judged by the rate of improvement in the bleeding time and platelet count cortisone did not appear to hasten the recovery of our patient nor that of Schoen *et al.* (1956). This is not to say that corticosteroids may not be beneficial in this condition for in idiopathic thrombocytopenic purpura it is recognized that cortisone lessens the risk of haemorrhage often without producing any effect on the platelet count. In view of the not inconsiderable risks of haemorrhage during the first week of life it seems desirable to treat these infant patients with corticosteroids.

The result of exchange transfusion in our patient is disappointing and suggests that this procedure may not materially alter the natural course of the disease. A final assessment of the therapeutic value of both exchange transfusion and corticosteroids must, however, await the publication of detailed studies on more patients.

Summary

A case report of a baby with congenital thrombocytopenic purpura is presented. The baby's mother had had a splenectomy for idiopathic thrombocytopenic purpura 20 years previously. The infant was treated by exchange transfusion and corticosteroids.

Platelet agglutinins which were demonstrated in the serum of mother and baby shortly after birth could not be identified in the baby's serum at 26 days. The thrombocytopenia, however, persisted and during the first three months the platelet count never rose above 120,000/c.mm.

Although the baby made an uneventful clinical recovery it is doubtful if therapy materially altered the natural course of the condition.

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TWO OUTBREAKS OF NEONATAL SKIN SEPSIS CAUSED BY *STAPHYLOCOCCUS AUREUS*, PHAGE TYPE 71

BY

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Specific epidemic types of *Staphylococcus aureus* have been shown to be responsible for several outbreaks of pemphigus neonatorum (Elliott, Gillespie and Holland, 1941; Hobbs, 1944; Allison and Hobbs, 1947; Williams, Sims-Roberts and Cook, 1947; Parker and Kennedy, 1949; Miller, 1950; Rountree, Heseltine, Rheuben and Shearman, 1956; Gillespie, Pope and Simpson, 1957).

In this communication two further outbreaks in separate hospitals caused by *Staphylococcus aureus* phage type 71 are reported. The organisms were also isolated from a member of the nursing staff in each hospital.

Methods and Materials

Swabs were taken from the skin lesions of all the affected babies and from the anterior nares of both mothers and nursing staff. The swabs were cultured on blood agar anaerobically and aerobically. Saline moistened swabs were used for sampling the environment of the affected babies.

The Outbreaks

Hospital I. This hospital contains a maternity ward of 25 beds, eight of which are in one ward, and the remaining 17 are in small rooms of two to four beds. The unit deals, in the main, with emergencies, and some of the patients are discharged within 48 hours of delivery owing to pressure on beds. Normally the babies are with the mothers but, in view of the emergency nature of much of the work, some infants are often moved into a nursery.

For some time before the outbreak under discussion, all babies were dusted daily with hexachlorophene powder, and the incidence of sepsis among the babies had been low. During the two weeks preceding the first case, there had been two trivial examples of 'sticky eyes' and on May 13, Case 1, then aged 8 days, developed mild ophthalmia and two days later mastitis which proceeded to an abscess requiring incision. Mother and child were isolated and no further cases occurred until May 20, when Case 2, 12 days old, delivered by caesarian section, developed a septic blister behind the right ear. This was complicated by a submental abscess which required incision.

The department was closed to further admissions, but subsequent infections occurred as follows:

May 22. Case 3, 5 days old; sticky left eye; two blisters on right arm, one behind right ear, and one in left axilla.

May 23. Case 4, aged 5 days; paronychia right thumb; blister left thumb; septic spot left cheek.

Case 5, 3 days old; blister adjacent to umbilicus.

May 24. Case 6, 6 days old; small blister under chin.

May 25. Case 7, aged 4 days; umbilicus moist with adjacent blister.

Case 8, aged 6 days; blister left little finger; two days later, blister left nostril.

Case 9, aged 7 days; blister right index finger.

May 27. Case 10, aged 10 days; septic spot left leg, followed by several others on right leg and groin.

Case 11, twin of infant 10; oedema of left lower eyelid with associated blister; blister on forehead.

Case 12, 4 days old; blister left lower eyelid and lower lip, followed by another on cheek.

May 28. Case 13, 4 days old; multiple small blisters and spots on chin, blister on left hand; later, blister on right shoulder and middle and ring fingers of right hand.

Case 14, 4 days old; blister on right ear; later, blisters in both axillae, left groin, on the neck and left ring finger.

(The maximum extent of the disease is recorded in each case.)

None of the babies affected was seriously ill, and all responded well to treatment.

Hospital II. This hospital has a maternity department of 40 beds, divided into three wards of (*a*) 19 beds, (*b*) nine beds, and (*c*) 14 beds. The second of these, ward (*b*) has two labour wards, and patients from ward (*c*) are brought down to (*b*) to be delivered. As soon as they are fit enough, they and their babies are taken back to their original ward on the floor above. Thus ward (*b*) is exposed to a good deal of traffic, and this ward was the only one in which infection occurred. All babies are nursed with their mothers, and each ward is of the open type.

There had been no example of neonatal infection in ward (*b*) for some weeks before August 1959. The ward had, however, been unusually busy just before the first case appeared (on August 5 and 6, 17 women had

been delivered) and, for some time, the average duration of stay had been reduced to about four days. Infant care is much the same as in hospital I, but there are fewer trained staff available.

On August 7, Case T (born by caesarian section seven days before, birth weight 4 lb. 13 oz.) developed a blister on the right forearm. She was removed from the ward and, on the next day, a fresh blister appeared behind the left ear. On August 9, despite treatment, multiple blisters of the trunk and limbs developed, and were associated with widespread desquamation, resembling Ritter's disease. Nikolski's sign was present. At first the disease appeared to respond to treatment (penicillin, followed by aureomycin and erythromycin). On August 13, deterioration set in, the temperature rose for the first time and signs developed in the lungs. She died quite suddenly on the same day aged 13 days. Necropsy revealed confluent bronchopneumonia from which *Staphylococcus aureus* was isolated.

On August 7, Case R (also born by caesarian section on July 31, birth weight 8 lb.) developed paronychia of the right ring and both little fingers. He was removed to the isolation ward. On August 10, a small blister appeared beside the umbilicus. No further lesions were seen and he made a good recovery.

After the occurrence of the second case, ward (*b*) was closed. All patients at risk were followed, but no other cases of infection were seen.

The sources and sites of the infection in the two Hospitals are given in the Table.

TABLE
SOURCES OF *STAPHYLOCOCCUS AUREUS*, PHAGE TYPE 71

Source	Site	Hospital
Case 3	Skin bullae	I
Case 4	Skin bullae	I
Case 5	Skin bullae	I
Case 7	Skin bullae	I
Case 12	Skin bullae	I
Case 13	Skin bullae	I
Case 14	Skin bullae	I
Sister W.	Nasal mucosa	I
Saline swab	Window ledge	I
Saline swab	Partition	I
Case T	Skin bullae	II
Case R	Skin bullae	II
Mrs. T	Nasal mucosa	II
Sister T.	Nasal mucosa	II

Management

The organism isolated was found to be penicillin sensitive in all except one infant. Penicillin was therefore given to all except the most mildly affected. The skin lesions were treated with local applications of flavine or gentian violet in spirit. The latter seemed to be rather more effective. The carriers were treated with graneodin applied to the anterior nares, and excluded from duty until their nasal swabs were clear. When the second cases occurred, the practitioners attending infants discharged subsequently were asked to notify the hospital if any infection developed in either mothers or their infants. Only one such came to light, a single spot which rapidly disappeared. The wards concerned were closed to further admissions and the walls thoroughly cleaned, using 1:30 'savlon'. Following this, redecoration was undertaken.

The blankets and mattresses used were stoved. Subsequently, cotton cellular blankets were introduced. The use of hand creams and soaps containing chlorohexidine was encouraged. It is our impression that, following these outbreaks, there is greater awareness of the possible dangers amongst the nursing staff, and there have been no further cases.

Results

The first infant to be delivered in Hospital I was the only sufferer who developed no skin lesions. There is no proof that this baby was infected by the same strain of *Staphylococcus* as that cultured from many of the others. All the other infants showed the remarkably similar clinical picture described later.

In Cases 2, 8, 9, 10, *Staphylococcus aureus* phage type 71 was not obtained, possibly due to the habit, subsequently discouraged, of discarding the plates after one colony had been picked. In Cases 12 and 13, the strains were lysed by other dilute phages of Group II at 1,000 × R.T.D. Parker, Tomlinson and Williams (1955) regard these as 'normal 71' strains.

Discussion

In both these outbreaks, the majority of the staphylococci isolated from the lesions were of the same phage type. In Hospital I, a single carrier was detected. In Hospital II, the mother of Case T who, together with one of the ward sisters alone among the adults at risk, was found to be harbouring the particular strain of *Staphylococcus aureus*, may have been the culprit. Nasal swabs from the affected sister had never previously yielded *Staphylococcus aureus* phage 71. Subsequent swabs have been negative. Two points require emphasis. First, phage type 71 had never previously been found despite the occurrence of minor staphylococcal infection and the previous isolation of the *Staphylococcus aureus* from nasal swabs, blankets and dust and, second, the great similarity in the clinical appearance. The skin lesions were very alike and started as a small superficial pustule which spread to form a bleb which quickly desquamated, leaving a raw, red, slightly moist area. In some instances the initial finding was a minute spot beside the finger nail, which soon became a paronychia, often spreading to form quite a large blister. Sometimes more

than one finger was involved simultaneously. None was seen on the toes.

There can be little doubt that *Staphylococcus aureus* phage type 71, was responsible for the cases of pemphigus. Though Gillespie *et al.* (1957) reported similar findings in Bristol, it would be unwise to regard this particular phage type as being responsible always for the clinical condition described. Elek (1959) regards phage susceptibility and pemphigus-producing quality as being two independent biological entities. This association might be entirely fortuitous. Indeed, other phage types, particularly 80, have been responsible on other occasions, both in Australia (McLean, 1956; Clarke, McGeoch and Sippe, 1956; McCartney and Yates, 1956) and also in England where it has been 'frequently identified' (Elek, 1959). Nevertheless, it seemed to us of interest to record two further examples in which *Staphylococcus aureus* phage type 71 was once more an aetiological agent.

Summary

Two outbreaks of pemphigus neonatorum due to *Staphylococcus aureus* phage type 71 are described. In both outbreaks carriers in the nursing staff were incriminated. Some methods of management are detailed.

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NEONATAL AND MATERNAL SERUM TRANSAMINASE ACTIVITY AT BIRTH

BY

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Serum transaminase studies in adults have been widely covered in the medical literature and variations in their activity are well established in medicine particularly in relation to heart, liver and skeletal muscle disease. Wróblewski (1959) stressed the value as a diagnostic aid of increased transaminase activity when correlated with the clinical pattern. Kove, Goldstein and Wróblewski (1957 a, b) also studied the serum glutamic-oxalacetic transaminase (GOT) activity in the neonatal period. These workers estimated the serum GOT activity in 63 normal full-term newborn infants up to 11 days after birth and included nine cord blood estimations; this study of Kove *et al.* (1957 a, b) showed a wider physiological range than found in normal adults and recorded a normal range in the newborn period from 13 to 105 units with the exception of one infant in whom a level of 160 units was recorded. The cord blood estimations showed a lower range of GOT activity than in the older neonatal cases studied. The same workers in a further study estimated the activity of serum glutamic-pyruvic transaminase (GPT) in 63 newborn infants in the first week after birth and considered values up to 90 units as being normal in this age group. In this series nine cord blood estimations were also included and these showed levels varying from 12 to 40 units. Knutson, Cornatzer, Moore and Nelson (1958) studied GOT activity during pregnancy and found that normal pregnancy did not appear to influence the activity level.

The study being presented in this paper is a further attempt to establish physiological limits of serum GOT and GPT activity in mothers and their newly-born infants. Cord blood specimens were studied and the maternal blood samples were taken at the time of delivery. This study was done on a series of 19 European and 26 Bantu cases. Tables 1 and 2 record the findings in these groups; they include the maternal age and parity and the infants' birth weight and sex in addition to the serum GOT and GPT activity levels. The method of estimating the levels of enzyme activity was that described by King (1958).

The 19 European cases included 11 first pregnancies, six mothers with one previous child, and two having had three and four previous pregnancies. There were nine females and 10 males in this series and one premature infant weighing 4 lb. 13 oz. was included.

In the 19 European cases as listed in Table 1, 16 showed the serum GOT values to be consistently higher in the cord bloods of the infants than in their mothers at birth. Fourteen of the cord blood values were above the normal upper limits indicated by Kove and his colleagues and in eight of the mothers their values were above the generally accepted normal values.

The serum GPT activity ranges in cord blood were all, with the exception of two cases, below the normal upper limit level of 90 units suggested by Kove and his colleagues; our study recorded a range of 10 to 61 units with the exception of the two cases of 116 and 102 units, both in male infants. The maternal range of serum GPT activity was from 10 to 98 units with a single exception of 134 units.

The 26 Bantu cases studied included eight first pregnancies, nine with one previous pregnancy and the remainder with two and three previous pregnancies; the series included 16 male and 10 female infants with birth weights ranging from 5 lb. 3 oz. to 9½ lb.

These cases showed 11 cord blood GOT values above the levels of activity suggested by Kove *et al.*; the range in the whole series varied from 35 to 190 units. The mothers' levels were all 100 units or less with four exceptions. The GPT levels in the cord blood studies in this group ranged from 15 to 78 units and the mothers from 10 to 75 units with one exception of 118 units.

In both groups studied there were many fairly high GOT levels in cord blood specimens above

TABLE 1

SERUM GOT AND GPT ACTIVITY LEVELS IN 19 EUROPEAN MOTHERS AND THEIR NEWLY-BORN INFANT'S CORD BLOOD

European Cases	Maternal Age (years)	Parity	Birth Weight (lb. oz.)	Sex of Infant	Maternal Serum GOT Units/100 ml.	Infant Serum GOT Units/100 ml.	Maternal Serum GPT Units/100 ml.	Infant Serum GPT Units/100 ml.
1	18	Primip	7 7	F	60	110	30	35
2	38	3	6 8½	M	95	202	17	116
3	26	Primip	8 2	F	98	150	15	10
4	20	Primip	7 6½	M	119	185	98	47
5	20	Primip	6 10	F	255	190	10	30
6	24	1	9 13½	F	40	139	40	61
7	17	Primip	4 13	F	106	80	11	29
8	20	Primip	7 6½	M	119	185	98	47
9	22	Primip	6 12½	M	60	140	27	28
10	21	1	6 14½	F	146	148	38	40
11	28	1	7 7½	F	80	90	30	58
12	18	Primip	6 4	M	39	205	26	28
13	27	1	6 11½	F	64	110	50	50
14	21	1	8 6	M	60	83	58	60
15	20	Primip	7 14½	M	160	133	134	34
16	37	4	6 14	M	60	80	50	20
17	23	Primip	6 9½	F	60	105	50	46
18	27	1	6 15	M	131	170	60	102
19	21	Primip	7 5½	M	130	187	20	20

TABLE 2

SERUM GOT AND GPT ACTIVITY LEVELS IN 26 BANTU MOTHERS AND THEIR NEWLY-BORN INFANT'S CORD BLOOD

Bantu Cases	Maternal Age (years)	Parity	Birth Weight (lb. oz.)	Sex of Infant	Maternal Serum GOT Units/100 ml.	Infant Serum GOT Units/100 ml.	Maternal Serum GPT Units/100 ml.	Infant Serum GPT Units/100 ml.
1	24	2	7 4½	M	40	80	10	20
2	27	Primip	7 13½	M	80	85	30	30
3	23	Primip	5 15½	F	75	100	18	45
4	24	1	7 6	M	80	190	25	72
5	26	3	8 8	M	120	100	65	18
6	18	Primip	5 3	F	82	130	29	28
7	19	1	7 13	F	140	165	40	30
8	22	1	6 9	M	40	100	35	40
9	27	3	7 9	M	85	120	40	20
10	25	2	5 13½	F	70	110	20	30
11	20	1	6 8	F	150	90	25	40
12	15	Primip	9 8	M	42	70	15	25
13	23	3	8 2½	M	75	115	32	20
14	22	1	8 8	F	130	35	30	50
15	26	2	5 13	F	90	180	23	55
16	19	Primip	6 5½	M	78	128	28	52
17	26	3	5 12	F	100	90	40	20
18	23	1	8 2	M	80	90	50	65
19	20	1	6 1	F	80	90	75	78
20	20	2	7 4	M	75	90	118	30
21	19	Primip	8 2	M	85	165	24	25
22	29	2	7 8	M	65	132	23	35
23	29	1	8 2	F	70	105	30	30
24	18	Primip	6 7	M	75	165	16	30
25	18	Primip	6 7	M	70	70	35	15
26	26	1	6 12	M	75	100	25	30

the suggested upper limit of normal; it is suggested by this study on normal infants that they may show higher GOT values on cord blood specimens than previously accepted.

Summary

A study is presented of serum GOT and GPT activity in the cord blood of normal newborn European and Bantu infants and their mothers at the time of birth; the ranges of activity varied between the limits as recorded in the accompanying Tables and showed a higher range of GOT activity in cord blood samples of normal newborn infants than previously recorded.

The authors wish to acknowledge their gratitude to Professor O. S. Heyns, Drs. J. H. S. Gear, F. Daubenton, L. G. R. van Dongen and J. M. Samson for providing facilities to undertake this study. They wish to thank the Nursing Staff of the Labour Ward, Queen Victoria Maternity Hospital and the Bridgman Memorial

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FOETUS IN FOETU AND THE RETROPERITONEAL TERATOMA

BY

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Foetus in foetu, a descriptive term attributed to Meckel (*circa* 1800), should be applied only to those rare cases where a parasitic twin is found included within the abdomen of its partner. Lord (1954; 1956) reported two definite cases and reviewed other possible cases.

In contrast, the variety of teratoma which occurs in the retroperitoneal space is much less defined. Since the description of the first recognizable case by Dickinson (1871), an increasingly complex volume of literature has accumulated. Palumbo, Cross, Smith and Baronas (1949) documented many of the earliest cases of retroperitoneal teratoma and their work drew together some of the facts concerning a condition which they rightly say is seldom discussed in the medical reference volumes. Charles (1953) traced 82 case reports in the literature and since this time at least five further reports have appeared including some from Russia and Bulgaria. Many theories of origin have been suggested, with some authors contending that the teratoma represents a form of included twin. Although this is now unacceptable, it has resulted in the description of many retroperitoneal teratomas in confusing terms.

Willis (1958) pointed out the separate nature of the retroperitoneal teratoma and foetus in foetu, emphasizing that the former is a true tumour while the latter is not. However, as both conditions occur in the upper part of the retroperitoneal space, it is not surprising that terms such as 'foetus in foetu', 'parasitic twin' and 'suppressed twin' have been misapplied to teratomas having a marked degree of differentiation and some foetiform characteristic. Indeed, Willis concedes that final classification may be difficult, though he does not admit that the overlap of certain features implies that the two conditions are the same.

The purpose of this report is (1) to describe a further case where borderline pathological features are present; (2) to discuss and compare briefly the pathology of foetus in foetu and retroperitoneal teratoma and (3) to discuss their symptoms, physical signs, diagnosis and treatment.

Case Report

K.J., a 4-week-old female infant, was admitted to the Department of Child Health, Llandough Hospital, Cardiff, on October 18, 1958. The provisional diagnosis by the referring practitioner was 'intussusception'. The mother stated that the infant, who hitherto had been quite normal, had had vomiting after feeds, apparent abdominal pain, and green loose motions for 24 hours.

Birth weight was 7 lb. 5 oz. and gain had been normal. She was breast fed initially, but changed to artificial dried milk after 10 days. Pregnancy and delivery of the mother had been normal. The family was otherwise healthy and there was no history of previous twin pregnancies.

On clinical examination, the infant appeared well nourished and healthy. Weight was 8 lb. 6 oz. There were no signs of dehydration, anaemia or jaundice. A 'strawberry' naevus was present on the lateral aspect of the right thigh. The abdomen appeared slightly distended in the right upper quadrant, and in this region, extending across the midline, a firm, immobile, circumscribed mass was palpable. The liver could be separately palpated a finger's breadth below the costal margin. Bowel sounds were increased. Rectal examination was negative.

In the early consideration of the diagnosis, a retroperitoneal tumour was thought likely. A barium enema examination performed immediately was found to be normal. An excretory pyelogram showed normally situated and functioning kidneys, with a bifid pelvis on the right side. During these examinations abnormal calcification was noted above the pole of the right kidney. Further postero-anterior and lateral views demonstrated a chain of solid calcification in this region. While exact interpretation was not possible at this time, the presence of this calcification appeared to favour the diagnosis of retroperitoneal teratoma.

Blood group was A Rh+; Hb 80% (11·8 g.); white blood cell count, 21,000/c.mm.; corrected erythrocyte sedimentation rate, 39 mm./hour. A urine specimen was found to contain pus cells and organisms identified as *Esch. coli*. A stool examination for pathogens was negative.

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The intercurrent urinary infection was treated with nitrofurantoin for five days with satisfactory response.

Twelve days after admission, laparotomy was performed through a right paramedian incision (Mr. D. B. E. Foster). The exploration revealed a retroperitoneal tumour approximately 2 in. (5 cm.) in diameter lying somewhat to the right of the midline, between the diaphragm and the third lumbar vertebra. The liver and its hilar structures, the duodenum and the pancreas were displaced forwards by the mass. After mobilization of the duodenum and transverse colon medially and downward, the capsule of the mass was opened with the release of a little reddish brown fluid. The contained mass was easily removed, and after careful dissection the capsule was also excised. The abdomen was closed in layers without drainage.

Postoperative course was uneventful and normal feeding was rapidly re-established. When discharged from hospital on the ninth postoperative day the infant weighed 9 lb. 12 oz. The patient has shown normal progress when seen in the follow-up clinic.

Pathological examination of the specimen was carried out by Dr. F. K. Storing. 'Macroscopically: The specimen consisted of a parasitic foetus showing small imperfectly developed extremities. A separate specimen labelled capsule was also examined. Microscopically: Sections taken from the interior of the trunk part of the specimen showed heterogeneous arrangement of a variety of tissues and cells, including muscle fibres, fat, cartilage, intestinal mucosa, glands and nerve fibres. The appearances were typical of an adult teratoma. The capsule consisted of very vascular connective tissue embedded in which were ganglion cells, nerve fibres and scattered lymph follicles.'

Further detailed examination carried out in conjunction with Dr. Storing, showed other interesting features. Apart from the rudimentary limbs (Figs. 1, 2 and 3), a head and hind end could be identified. The lighter coloured band which can be seen projecting from the ventral surface of the specimen was thought to represent an umbilical cord. Radiographs of the specimen (Fig. 4) demonstrated rudimentary development of a spinal column and rib cage. Some calcification could be seen in one of the limbs.

Pathology

The main features of foetus in foetu and retroperitoneal teratoma will be described and comparison drawn where necessary. Preliminary acknowledgment is made to Lord and Willis, since due to their efforts a clearer understanding of the two conditions has emerged from a confusing and conflicting mass of fact and theory.

Nomenclature, Definition and Classification. Foetus in foetu has become an accepted term, which well describes a fascinating condition. As has been suggested, the names parasitic twin and included twin may equally well be used, provided the lingering association with teratoma is not propagated. The condition may be defined as a vertebrate foetus included within the abdomen of its partner. No further classification is necessary, though it can be mentioned that earlier writers described intra-abdominal and extra-abdominal types. No recent case of the latter, however, has been substantiated.

The retroperitoneal teratoma adopts the nomenclature, definition and classification of teratomas in general. A number of alternative names have been given to these tumours. These include 'teratoid tumour', 'terato-blastoma', 'teratocarcinoma' (when malignant) and 'embryoma'. Willis (1958) rejects these on various grounds and further condemns the use of the term 'dermoid cyst'. He states that apart from confusion which may occur with the sequestration dermoid cyst, even the simplest teratomatous 'dermoid cyst' contains a second tissue, and may be lined with tissue other than skin. A teratoma is defined as a true tumour or neoplasm composed of multiple tissues of kinds foreign to the part in which it arises. A wide range of classifications have been adopted, based on the physical or microscopic characteristics of the tumour. The use of the simple division, solid and cystic, may be criticized on the grounds that all teratomas exhibit a relative degree of these features. The names monodermona, bidermona and tridermona have been used having relation to the proportion of the constituent tissues arising from the three germ layers. It is felt that this is a clumsy way to describe a tumour which almost always contains several types of tissues. Most commonly teratomas are classified as adult or embryonal, according to the maturity of the cells in the tumour. From the same evidence a tumour may be labelled benign or malignant. Owing to the varying characteristics of these tumours and even a single tumour, none of these classifications is entirely satisfactory. No further doubt should remain, however, that foetus in foetu and retroperitoneal teratoma refer to different conditions.

Incidence. Lord (1956) found 31 reports of alleged foetus in foetu before 1900 and 11 reports since that year. Of the 11 more recent cases only four had unequivocal evidence of the condition.

The retroperitoneal teratoma is also a rare condition, being recognized in only 10% of all retroperitoneal primary neoplasms. It is also a fairly uncommon member of the teratoma family; in order of frequency of occurrence the various sites are ovary, testis, anterior mediastinum, retroperitoneum, sacrum, coccyx, cranium and neck.

FIG. 1.

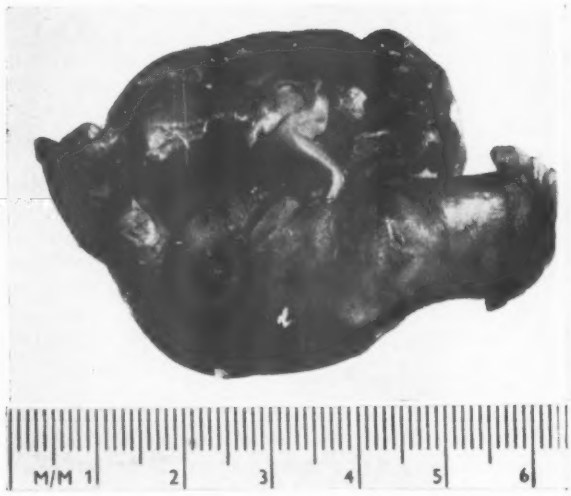

FIG. 2.

FIG. 3.

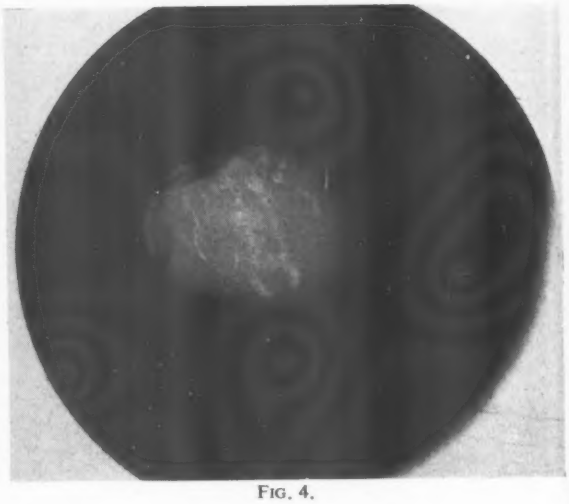

FIG. 4.

FIGS. 1 and 2.—General views of the specimen.

FIG. 3.—Close up view of digits of one lower limb.

FIG. 4.—Radiograph of specimen.

Age and Sex Distribution. More than 50% of all retroperitoneal tumours manifest themselves in early life.

Practically all the reported cases of foetus in foetu were noted in the first 12 months of life, usually in early infancy.

In the case of retroperitoneal teratoma, Palumbo *et al.* (1949) stated that the average time of diagnosis was at 13 years; 55% were said to have been diagnosed in the first decade of life, while 30% were found in the first year of life. Cole and Gerrish (1951) reported removing a retroperitoneal teratoma

15 hours after birth, while at the other extreme a similar tumour has been removed from a patient aged 53 years.

There is no indication of any particular sex incidence in either condition. Gross and Clatworthy (1951) made the observation that while the sex incidence in retroperitoneal teratoma is nearly equal, in sacrococcygeal teratomas there is a four to one preponderance toward occurrence in females.

Site of Occurrence. The upper part of the retroperitoneal space is the only site of occurrence of foetus in foetu. No case has been reported in the pelvis or in any abdominal organ. Previous writers have described the occurrence of foetal structures within the brain, abdominal wall and the uterus. A particular case is that of Kimmel, Moyer, Peale, Winborne and Gotwals (1950). In this instance, there was a cerebral tumour allegedly containing five human foetuses. However, doubt exists whether these fully meet the requirements to classify as included quintuplets, and discussion still continues.

The foetus in foetu is usually suspended by a peduncle within a capsule containing a little fluid. The wall of the capsule is often thickened at the point of attachment of the peduncle with an associated plexus of vessels. The thickened part may be orientated toward the base of the mesentery and the origin of the superior mesenteric artery. No direct connexion of peduncular vessels with those of the host has been shown, in the cases where this examination has been possible.

The retroperitoneal teratoma also more commonly occurs in the upper part of the retroperitoneal space. Arbitrarily dividing the space into left and right compartments, with the spinal column forming the median boundaries, this type of teratoma is said to occur twice as frequently on the left side. Most are located in an immediate paramedian pre-axial position.

The retroperitoneal teratoma is typically without a capsule or pedicle, and attachment to the posterior abdominal wall is broad and intimate. The area of attachment may be in close relation to the upper pole of the kidney, the pancreas or the coeliac axis of vessels. Growth of the tumour may displace any related organ with resulting distortion of the anatomical situation.

Macroscopic and Microscopic Appearance. The outward appearance of the foetus in foetu may vary from an anencephalic globular or reniform mass, with rudimentary limb buds, through all stages of development to the well-formed foetus. More than one part of a foetus should always be recognizable and the suspending cord or peduncle should also be identifiable.

Internally, a vertebral column at some stage of development will be found, together with other bones. A complete foetal skeleton may exist. Of the soft tissue structures, the intestinal tract is usually best represented. Various other organs may be recognizable including brain, spinal cord, lungs, gonads and adrenals. A rudimentary cardiovascular system may be present, but this is not functional and the foetus is acardiac, deriving its blood supply from its host. The enclosing capsule usually consists of connective tissue with a lining endothelium which may be stratified squamous in type. No trophoblastic or placental tissue has yet been described in the capsule.

The gross and histological features of the teratoma are well known. The tumour may reach a very large size and one weighing 26 lb. has been reported. This is in contrast to the foetus in foetu which remains quite small. Occasionally a well-formed foetal part may be found within the teratoma, such as a single digit. An instance of this was described by Krug (1956). The formation of a vertebral column and the occurrence of segmentation is unknown.

Microscopically, multiple different mature and immature tissues will be observed, with no evidence of organ-like arrangement. It is interesting, however, that some tissue correlation does occur. For example, teeth may be set in bony sockets and may even erupt into cystic cavities, alimentary mucosa may be related to smooth muscle, and respiratory tissue to cartilage. In explanation, Willis (1958) suggests that contiguous tissues may exert an inductive effect on one another. In malignant teratomas abundant immature embryonic cells will be seen, having marked proliferative and invasive properties.

Growth and Malignancy. The foetus in foetu, commencing existence as a true twin, grows initially in parallel with its fellow. Soon, however, because of its anatomical confinement and perhaps some other factor which determined its parasitic role, it lags behind its host. From the latter it becomes dependent for its blood supply, and does not develop a functioning heart and circulation of its own. Although the limbs of the included foetus may appear to be well developed, their ratio to trunk is behind that of a similar age normal foetus. After attaining a variable size, further growth ceases, and actual retrogression can occur as the host twin progresses. Willis (1958) describes in detail

how reduction of a parasitic twin may be brought about, with loss of head, limbs and internal organs. It is not, however, certain whether the factor involved is the vascular dominance of the host twin, or some inherent defect in its parasitic partner which causes these changes. It thus becomes evident that the extensively reduced foetus may be distinguishable only with difficulty from a teratoma. There is no evidence, however, to suggest that the foetus in foetu can become anything but a quiescent malformation, and therefore has no neoplastic or malignant propensities.

Quite oppositely, the retroperitoneal teratoma is characterized by progressive growth. It probably arises at an early stage in prenatal development and will have been present for a long period before discovery in infancy, childhood or later life. Maturation of tissues in the tumour may continue apace with those of the host. In fact maturation may become complete and the tumour become quiescent. The presence, therefore, of relatively immature tissues in the tumour of a small infant may not be a sign of malignancy. The observation of such cells or tissues in the teratoma of an adult, however, would have serious implications.

Immediate recognition of malignancy may be difficult. It is probable that more than the accepted 10% of retroperitoneal teratomas are malignant at time of operation. Metastases are frequent and may occur in the lungs, liver and vertebrae. If the parent tumour is actively proliferating, for example in a young patient, then the metastases will be composed of mixed cells and tissues. If, however, in an adult type tumour one element becomes malignant, then the metastases will be of this tissue.

Pathogenesis. The foetus in foetu is a monozygotic twin. Developing from a single ovum, it would, but for the limitations in growth which occur later, be of the same sex and closely resemble its host. It is not proposed to discuss the phenomenon of twinning, apart from recalling the strong hereditary tendency, and noting that the membranes may be shared to a varying degree by the developing foetuses. Early cleavage of the dividing cell mass may so occur that each may have its own chorion, or that this may be shared. It is then likely that each foetus will have its own amniotic cavity. Occasionally the twin embryos appear at a later stage and a common amniotic cavity is utilized. Willis (1958) states that most if not all conjoined twins and double monsters are in this group. While it would be possible to theorize that even later cleavage into twins might result in the inclusion of the second embryo within the body layers of its partner, there is no supporting evidence for this, and for that matter no other reason for foetal inclusion has been suggested.

In contrast to the foetus in foetu, very much has been written about the pathogenesis of the retroperitoneal teratoma and teratomas in general. Many theories have been put forward, both complex and conflicting. Most attempt to relate the development of a teratoma to some form or gradation of twin development, or the parthogenetic stimulation of sex or dislocated germ cells. These views should now be discarded. Teratomas should not be considered as incomplete or distorted foetuses within a host, nor the result of fertilization of an ovum within a foetus or infant.

Spemann (1938) first postulated that a 'primary organizer' determined the orderly development and growth of embryonic tissues into the normal structure of the human body. Askanazy (1908) had already indicated that teratomas must arise from abnormal tissue primordia in early embryonic life, while Budde (1926) first suggested the theory that teratomas result from disturbances in the primitive streak. Needham (1936; 1942), Nicholson (1935) and especially Willis (1935; 1937; 1953) endorsed, expanded and nurtured the theory that teratomas were derived from cells related to the invaginating primitive streak, which escaped organizer influence.

In summary, it may be concluded that the retroperitoneal teratoma (or any teratoma) is congenital, and arises in a median or paramedian location from embryonic pleuripotential cells associated with the primitive streak. These cells, uninfluenced by the primary organizer, form a true neoplasm, which may later exhibit benign or malignant characteristics.

Symptoms, Signs, Diagnosis and Treatment

Foetus in foetu and retroperitoneal teratoma may present in essentially the same fashion. Certain variations do occur and these will be indicated. In a similar way diagnosis and treatment may be considered concurrently.

Symptoms and Signs. These are due to the pressure effects of the tumour, and while initially vague, become increasingly persistent as the tumour enlarges. This is especially so in the case of retroperitoneal teratoma where pressure effects tend to be more severe.

The infant may present with feeding difficulties, vomiting, constipation, weight loss, dyspnoea and pain. Alternatively, abdominal distension with an accompanying abdominal mass may be noticed first.

This is more likely to be the case in older patients having a retroperitoneal teratoma. The mass is usually circumscribed, sometimes mobile and may feel lobulated or cystic. Dilated veins may be seen beneath the skin of the abdominal wall and the extremities may exhibit secondary oedema. Sepsis in, or avascular necrosis of, a foetus in foetu may cause rapid increase in size of the tumour, with pyrexia and possibly signs of peritoneal irritation.

Diagnosis. By a process of elimination the presence of a retroperitoneal tumour may be deduced and indeed it may be possible to specify foetus in foetu, or teratoma.

In infants, other conditions will require urgent exclusion. These include intussusception, Wilms' tumour and neuroblastoma. In older patients extensive investigation may be required to exclude gastrointestinal tract, pancreatic and renal tract lesions. Secondary abdominal lymph node deposits from a malignant testicular tumour may give rise to an abdominal mass, 'the epigastric tumour of Osler'. An associated pyrexia may influence the diagnosis toward a malignant tumour, primary retroperitoneal or otherwise, except in the circumstances already mentioned.

Plain radiographs of the abdomen may provide conclusive evidence. Apart from the position of the soft tissue mass on postero-anterior films and lateral films, and indentation or displacement of gas shadows, irregular calcification or actual bones may be seen. The presence of a formed foetal skeleton, or bones with vertebrate organization is strongly in favour of a foetus in foetu. It must be remembered, however, that calcification may occur in other degenerating tumours. Barium studies of the upper and lower intestinal tract may be necessary if the diagnosis is in doubt. An excretory pyelogram will serve to exclude a renal lesion. Normally functioning kidneys may be outlined, but the close proximity of a retroperitoneal tumour may cause one or the other kidney to be displaced forward and laterally.

Treatment. Surgical removal of the tumour should be carried out without undue delay. Cole and Gerrish (1951) commented that nothing was to be gained in small infants by procrastination, and reiterated that as time goes on the newborn infant becomes a poorer surgical risk.

If the diagnosis is reasonably certain, however, the removal of a foetus in foetu does not normally call for such urgency. In the absence of infective complications, which might induce peritonitis or a local adhesive reaction, a reasonable time for investigation and preparation may be taken. Depending on the age and condition of the patient and the anatomical relations of the tumour, it may be considered advisable to remove the foetus only, from within its sac.

On the other hand, the potentially malignant nature of a teratoma, and of other similarly situated tumours when the diagnosis is doubtful, calls for early operation. The patient and surgeon should be prepared for a lengthy and difficult procedure. Complete removal of all the abnormal tissue must be aimed at; otherwise local recurrence with possible subsequent malignant degeneration can occur. Preoperative preparation should include a chest radiograph and skeletal films, since distant metastases may have occurred already. Lord (1954) in her review of previous cases of foetus in foetu, observed that the prognosis was far better in this condition, than in teratoma, with or without surgical intervention.

Conclusion

An attempt has been made to separate the characteristics of two interesting conditions, often confused in the past. A further illustrative case has been described, which in the author's opinion was probably a foetus in foetu. Certain contradictions in the pathological description are evident. The internal histology of the specimen was manifestly teratomatous. Yet could this represent all that remained of the interior of a markedly reduced foetus? It is suggested that it may still be difficult to identify correctly borderline instances of these conditions, unless very minute and painstaking examination of the fresh specimen is carried out.

The author wishes to thank Professor A. G. Watkins, Department of Child Health, Cardiff, and Mr. D. B. E. Foster for permission to publish details of the case history; and Dr. F. K. Storing, Llandough Hospital, Cardiff, for his assistance.

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PAEDIATRIC PATHOLOGY CLUB

Proceedings of the Sixth Annual Meeting

The sixth meeting of the Paediatric Pathology Club was held in the Pathology Department of the Royal Hospital for Sick Children, Glasgow, on October 21 and 22, 1960, under the chairmanship of Dr. A. Macdonald. Twenty-two members and 21 guests signed the register.

The following papers were presented.

Summaries of Original Papers

T. E. PARRY (Cardiff). 'Aminoaciduria in Childhood Due to Causes Other than Liver Disease.' Four cases of phenylketonuria, one of cystinuria, one of the Fanconi syndrome, a case of dermatomyositis with severe malnutrition and two cases of unexplained aminoaciduria were investigated chromatographically.

Phenylalanine was demonstrated in the urine in all, and in the blood in two of the phenylketonurics.

The typical pattern of cystine-lysine-arginuria was demonstrated in the cystinuric after cystine crystals had been discovered incidental to infective hepatitis. Chromatograms of whole blood, plasma and packed red cells were normal. Aspartic and glutamic acids were present in higher and valine and leucine in a lower concentration in the packed cells than in the plasma. Glycine, serine, threonine, alanine, glutamine and tyrosine were present in about equal concentration in both. The distribution of amino acids between cells and plasma was identical to that observed by the author in normal subjects.

Two cases of generalized unexplained aminoaciduria were encountered. (1) A large male infant who died at 36 hours; hyperplasia of the islets of Langerhans was a striking feature at necropsy. The aminoaciduria was considered to be in excess of the physiological aminoaciduria at this age. (2) A boy of 2½ years with a history of 'fits' presented with unilateral cataracts. He was normal physically and mentally. He excreted large quantities of glycine, threonine, alanine, glutamine, valine and leucine with small quantities of histidine, tyrosine, phenylalanine and asparagine.

I. E. C. WILSON (Glasgow. Introduced by A. Macdonald). 'The Mode of Action of Dexamethazone and Chlorothiazide in the Treatment of Nephrotic Oedema.' The diuretic effect of dexamethazone and chlorothiazide in nephrosis was demonstrated in respect of water and electrolyte excretion. Chlorothiazide produced a marked diuresis within a few days with no remission of the albuminuria. Dexamethazone caused diuresis after a latent period of five to nine days. The albuminuria gradually diminished from the fifth to the ninth day. The diuresis preceded any increase in total protein or albumin in the serum. The concentrations and total excretions of Na and K at the commencement of the diuresis did not justify a conclusion as to whether it was due primarily to a diminution of an ADH factor or aldosterone secretion. A few experiments on animals indicated that dexamethazone depressed the excretion of an ADH (pitressin) factor.

O. H. WOLFF, A. H. CAMERON and H. B. SALT (Birmingham). 'Veno-occlusive Disease in Protein-losing Enteropathy.' A 2½ year-old boy presented with generalized oedema and gross enlargement of the liver. Liver biopsy suggested the diagnosis of veno-occlusive disease. It then came to light that the patient was in the habit of nibbling various plants, his favourite being groundsel (*Senecio vulgaris*).

The oedema was due to hypoproteinaemia with depletion of albumin and all the globulins, particularly gamma globulin. The hypoproteinaemia was found to be the result of a protein leak into the gut: after an intravenous injection of I^{131}-labelled polyvinylpyrrolidone (P.V.P.) 12·5% of the dose appeared in the faeces (Dr. W. F. R. Pover). On treatment with prednisolone the serum proteins returned to normal, the oedema cleared and only 1% of an intravenous dose of P.V.P. appeared in the faeces—a normal result. After 21 months of steroid treatment the patient still requires prednisolone to maintain normal serum protein levels.

Possible relationships between the protein-losing enteropathy and the veno-occlusive disease were discussed.

D. BIALESTOCK (Melbourne). 'Microdissection of the Kidney.' The historical background and technical details of the method of microdissection as applied to the infant kidney were outlined. Use of the method was demonstrated by slides of nephrons from cases of cystic disease, pyelonephritis, hydronephrosis and the nephrotic syndrome in babies.

The study of the nephron in its entire length in the baby reveals bizarre, multiple abnormalities and final interpretations of the significance of these in clinical manifestations are, as yet, not at all clear.

A. H. CAMERON (Birmingham). 'Intestinal Biopsy in Coeliac Disease.' Sixty-nine per-oral biopsies of the duodenum and jejunum have been performed at the Birmingham Children's Hospital in the past 18 months. By measuring the surface area and relating this to the

obliteration of the intervillous spaces a mathematical index of the degree of abnormality can be established. This has proved useful in the diagnosis and follow-up of cases of coeliac disease. Gluten-free diet improves the appearances and the index number becomes normal in about two-thirds of cases. Striking improvement is seen after five months' treatment. Clinical response to treatment is not always accompanied by histological response. Intestinal biopsy is regarded as the most reliable single investigation in coeliac disease and is a safe procedure even in young infants.

J. J. BODDAERT (Ghent, Belgium). 'The Pathology of Human Thyroid Aplasia with Special Reference to the Changes in the Endocrine Organs.' Two cases of congenital absence of the thyroid gland in female infants were studied. At necropsy no thyroid gland could be found. In one case, 3 months of age, the organs of the neck were studied completely on serial sections, while in the case aged 28 months numerous blocks of tissues were taken at both sides of the trachea for microscopical study.

In the region where the thyroid should have been found, groups of small cysts located laterally to the trachea were observed on microscopic examination. The cysts were closely associated with small islets of poorly differentiated 'thyroid' tissue and with the parathyroids, whose size and structure were normal.

The cysts and islets could be remnants of the lateral thyroid anlage contributing to the formation of the normal thyroid gland.

The following changes were observed in the endocrine organs: the pituitary was normal in weight but in both cases the acidophils were decreased and an increased number of sparsely granulated and degranulated modified acidophils resembling thyroidectomy cells was found. In addition, in the case aged 28 months, the basophils were increased in number.

The thymus was markedly atrophic. In one case (28 months) myoid cells with cross striations were present. The adrenals were of normal weight and morphology for this age.

The islets of Langerhans in the pancreas were large and in some instances hypertrophic. The ovaries contained atretic follicle cysts.

S. A. DOXIADIS, PH. FESSAS and T. VALAES (Athens, Greece). 'Glucose-6-phosphate Dehydrogenase Deficiency; a new aetiological factor of neonatal jaundice.' In about one-third of all cases of severe neonatal jaundice in Greece there is no Rhesus or ABO incompatibility. This type of jaundice not due to iso-immunization may cause kernikterus if not treated by exchange transfusion. Many clinical and laboratory features point to an increased postnatal haemolysis; there is also a familial incidence and a preponderance of males.

In their search for an inherited haemolytic factor they were able to show, using the technique described by Motulsky and Campbell, that the great majority of these babies had deficiency of the glucose-6-phosphate dehydrogenase of their red cells. The incidence of this enzyme defect in a group of controls was minimal. They postulate that G-6-PD deficiency may be an important aetiological factor of severe neonatal jaundice in some countries where this enzyme defect is prevalent.

A. MITHAL and J. EMERY (Sheffield). 'The Effect of Birth on the Heart Ventricles.' Diverse opinions are expressed concerning the growth of the right ventricle after birth. Authors that have shown right ventricular atrophy have used cases of doubtful maturity at birth and included wasted children.

After careful exclusion of pathological material and infants of uncertain gestation, ventricular weights from 122 children with ages from birth to 12 years were analysed. In children born prematurely the right ventricle continues to grow at the same rate as if the child had been *in utero*, but the left ventricle grows at a greater rate.

After full-term birth, the right ventricle continues to grow uniformly, there being no phase of atrophy.

R. F. JENNISON and F. A. LANGLEY (Manchester). 'Perinatal Lung Infection.' Previous work from St. Mary's Hospital has shown that three types of perinatal pneumonia can be distinguished:

(*a*) Foetal pneumonia, occurring in foetuses at or near term;
(*b*) Later perinatal pneumonia, in infants dying after the first day but before the second week;
(*c*) An intermediate type in infants dying during the first day.

The present investigation was undertaken to study the bacteriology of perinatal pneumonia in relationship to pathogenesis. After searing the surface of one lung a fragment was incubated in Brewer's medium and on a blood agar plate. A smear was also examined microscopically. The efficiency of this method of isolating organisms was estimated at about 91% and the 'laboratory contamination' rate at between 1·2% and 5·4%.

Organisms were found in only about half the lungs showing histological evidence of pneumonia. The possible reasons for this were discussed. During the period 1955 to 1959 organisms were found in about 18% of lungs which showed no pneumonia. This is termed 'pulmonary soiling'. Analysis of the types of organisms present shows that the flora in pulmonary soiling is similar to that of the parturient vagina and also of foetal pneumonia. The bacterial flora in later perinatal pneumonia can be resolved into two components: (1) That due to pulmonary soiling about the time of birth, and (2) that derived from the environment later, especially *Staphylococcus pyogenes* in the hospital.

P. D. HOLLAND (Dublin). 'Ward Trial of the Bacteriological Effect of Hexylresorcinol Aerosol.' Control air bacterial counts showed that about 30% of the air bacteria were potentially pathogenic staphylococci with antibiotic resistances comparable to those of organisms isolated from cross infections in the ward. Dust samples from each room and cubicle also were tested for antibiotic sensitivity.

After seven, nine and 14 days' exposure of the ward to the hexylresorcinol aerosol (Aerovap), air bacterial counts indicated a marked and sustained reduction of the bacterial air count in the central corridor of the cubicle ward.

The cubicles showed a reduction in bacterial air counts not as convincing as that in the central corridor, due probably to inadequate penetration of the aerosol.

Post-aerosol sampling showed that the dust flora had been favourably influenced by the aerosol.

Nasal swabs from the nursing staff showed no change in the percentage of carriers nor in the sensitivity of the strains isolated after 14 days' exposure to the aerosol.

No toxic effects were noted.

It is clear the hexylresorcinol aerosol is bactericidal and that its maximum effect is demonstrated where adequate air concentration can be maintained, i.e. in closed corridors and in individual rooms and cubicles.

K. B. ROGERS and N. SLATER (Birmingham). 'A New Method of Disposal of Soiled Nappies.' Nappies from babies in hospital, especially those of babies suffering from gastro-enteritis, may help to spread infection between the time when they are taken from the baby and when they arrive in the laundry and are placed in washing machines. A German technique has been adapted to solve this problem, using disposable polythene bags which are sewn along one side with an artificial protein thread.

Soiled nappies in these bags are transported to the laundry and are thrown unopened into a washing machine in which there is a solution of a proteolytic enzyme. In this the special protein thread is dissolved, allowing the bags to fall open. After a quarter of an hour, the contents of the washing machines are boiled. The effluent from this washing machine contains no viable non-sporing organisms. The proteolytic enzyme helps to remove adherent faeces allowing the nappies to be washed more easily and more efficiently than with conventional methods but eliminating much of the offensive odour associated with the washing of these soiled nappies. The enzyme, thread and the made-up bags are all now being manufactured in England.

R. A. OSBORN (Derby). 'Intestinal Perforation in Three Children with Polyarteritis Nodosa.'

Case 1: A boy, aged 8, was admitted with tonsillitis followed by melaena and a purpuric rash and later abdominal pain, haematuria and convulsions with a blood pressure of 160/100 mm. Hg. Laparotomy revealed 18 in. of gangrenous and perforated small bowel, with undermining ulcers and polyarteritis nodosa in the less affected areas. Progress was slow. Persistent haematuria and hypertension were treated with prednisone and mecylamine. He is now well and symptom free.

Case 2: A full-term normal girl was constipated and vomited after birth; a tight anal sphincter was dilated. Abdominal distension increased on the 11th day and fluid levels were seen in the erect radiograph of the abdomen.

A 4-in. segment of gangrenous splenic flexure of colon was resected. She died 10 hours after operation. Necropsy showed hard, brown faecal masses in the rectum and lesions of polyarteritis nodosa in the bowel wall and around the ovaries. There was calcification of striated muscle fibres in the diaphragm end of the distal convoluted tubules of the kidneys.

Case 3: A full-term normal girl whose mother was a diabetic. An infected umbilicus was treated with streptomycin. At 3 weeks she developed melaena with vomiting and a temperature of 102° F. She died one week after admission. Necropsy revealed a general peritonitis due to perforation of the jejunum. The small bowel showed numerous small ulcers. An abscess 1 cm. in diameter was present near the umbilicus. There was a large haemorrhage into the right adrenal. Polyarteritis nodosa was seen in the small bowel and adrenals. There were numerous venous thromboses in the kidneys and around the peritoneum. Calcification was present in the umbilical vessels and alongside the thromboses in the renal veins.

J. M. A. LENIHAN and J. M. WARREN (Glasgow. Introduced by A. Macdonald). 'Radioactive Strontium in Human Bone—Glasgow Measurements for 1959.' Radioactive strontium ^{90}Sr, produced in fall-out from distant nuclear weapon explosions, is being deposited over the earth's surface (more particularly over the Northern hemisphere) at the present time. Local concentrations depend largely on rainfall but ground contamination is otherwise fairly uniform between latitudes 40° and 60° N.

Some of the ^{90}Sr is incorporated in grass and other growing crops, from which it passes into animal and human food chains. Milk, vegetables and wheat products are the main sources in human diet.

A proportion (about 25%) of the ^{90}Sr ingested by an infant is incorporated in the growing bone. Present indications are that the amounts accumulated are well below the danger level, but long-term studies are clearly desirable. The amount of ^{90}Sr in an infant femur may be as little as 10^{-13} g. (0·1 $\mu\mu$g.). The separation of this material from the accompanying several grams of calcium is a difficult exercise.

The radioactive strontium is prepared as carbonate on a small planchet and assayed by a specially built low-background Geiger counter system.

During 1959, 125 bone samples (femur) were obtained. One hundred and three were prepared and assayed in Glasgow; 22 were analysed at Woolwich for comparison purposes.

Detailed studies of the 1959 results have been published by the Medical Research Council.

P. ROBB (Dumfries. Introduced by A. Macdonald). 'The Development of the Islets of Langerhans in Man.' The present study was based on 36 pancreases from foetuses ranging between 10 and 42 weeks' gestation and weighing between 34 g. and 3,600 g. Four stages were observed in the development of the islets; these over-

lapped, so that in any one pancreas, there were islets in more than one stage.

1. *Stage of budding islets:* In the third and fourth gestational month, islets consisting of a central cluster of B cells surrounded by ungranulated cells and occasional L cells, budded off from the ducts. The B cells predominated.

2. *Bipolar Stage:* From the fifth to eighth month, bipolar islets were seen, with the B cells at the tip and the L cells at the base (nearest the duct).

3. '*Mantle-islet*' *Stage:* The proliferating L cells grew round the B cells to form 'mantle-islets' with a kernel of B cells and a shell of L cells. The L cells now greatly outnumbered the B cells. 'Mantle-islets' dominated the picture from the sixth month onward.

4. *Stage of Mature Islets:* From the eighth month, a few islets were seen with the haphazard distribution of L and B cells characteristic of the mature adult islet.

A point of particular interest in these observations was the presence of differentiated L and B cells in the islets of the smallest (34 g.) foetus.

DOUGLAS BAIN (Edinburgh). Mast cells were obtained from the tissue culture of a tumour from a newborn infant. The tumour was multifocal and undifferentiated.

G. S. ANDERSON and T. BIRD (Newcastle). 'Congenital Iodopyrine (Felsol) Goitre.' Evidence recently presented by Morgans and Trotter (1959) strongly suggests that Felsol, a drug commonly taken by asthmatics, may be goitrogenic due to the iodopyrine it contains. Two infants (binovular twins) with congenital goitres, born of a mother with asthma and a goitre considered to be due to Felsol, were presented. One infant died at 10 hours with a thyroid of 11 g. showing large irregular vesicles filled with colloid but with signs of epithelial activity. The other twin died at 38 days with a thyroid weighing 7 g. showing small vesicles, poorly filled with colloid and a flat epithelium. It was suggested that the iodides liberated from iodopyrine in the maternal gut crossed the placenta to block the iodine-binding power of the foetal thyroids. Since Felsol was withdrawn nine days before delivery the histology was considered to support the view that iodides caused a colloid type of goitre, but that epithelial activity soon occurred when iodides were stopped. Neither death was attributable to the goitres.

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Morgans, M. E. and Trotter, W. R. (1959). Iodopyrine as a cause of goitre. *Lancet*, **2**, 374.

K. M. LAWRENCE (Cardiff). 'Sarcoma of Pelvis.' A large pelvic tumour that had invaded the bladder and grown along the inferior vena cava; it was thought to be an embryonic sarcoma, possibly a rhabdomyosarcoma originating from the prostate.

H. B. MARSDEN (Manchester). 'Metachromatin Leucodystrophy.' A male child with a normal sibling began to have attacks of pyrexia at the age of 16 months. He eventually lost the use of his arms and legs, developed opisthotonos and died after repeated fits at the age of 2 years 10 months. The E.C.G. showed generalized dyspolicythuria and the C.S.F. had a protein level of 100 mg. %.

At necropsy the brain appeared relatively normal to the naked eye, but showed extensive gliosis of the white matter. Sudanophilic material was minimal and present only as small perivascular collections.

On staining with toluidine blue abundant metachromatic material was present in the brain, peripheral and spinal nerves, kidneys and to a lesser degree, in the liver, pancreas and adrenal medulla. Clinical analysis of the brain (Professor J. N. Cunningham) revealed loss of phospholipid and cholesterol with increase of hexosamine in the white matter. Numerous needle-shaped crystals were found in the adrenal cortex.

J. L. EMERY (Sheffield). 'Congenital Hypothyroidism —presenting clinically as intestinal obstruction.' A child was described having a minute aberrant lingual thyroid only who presented clinically as intestinal obstruction ? congenital megacolon. Other instances of congenital thyroid deficiency presented in this way were referred to.

W. W. PAYNE (London). 'Apparatus and Method of Ultra Micro Chemical Techniques.' Description and demonstration.

Erratum

It is regretted that in the paper 'Observations on the Clinical Course and Treatment of One Hundred Cases of Still's Disease by B. E. Schlesinger, C. C. Forsyth, R. H. R. White, J. M. Smellie and C. E. Stroud, which appeared in this journal (Volume 36, pages 65-76) Figs. 9a and 9b were transposed.

BOOK REVIEWS

Year Book of Pediatrics (1960-1961 Year Book Series). Edited by SYDNEY S. GELLIS. (Pp. 479; 92 figures. 60s.) Chicago: The Year Book Publishers; London: Interscience Publishers. 1960.

Anyone glancing through this Year Book will gain a rapid insight into what has been going on in children's medicine during the year. All branches of the subject are considered and the reader will end his perusal as up to date in surgery and pathology as in internal medicine.

The doctor with limited time for reading and restricted in foreign languages may regret that the Year Book does not give him more insight into Continental literature. He may speculate whether the high proportion of American papers abstracted is a true reflection of where most of the worthwhile new work is being done. He cannot but be grateful to the editor, however, for enabling him to do his year's reading in a rapidly progressing subject so agreeably in a couple of evenings.

Dr. Gellis is to be warmly congratulated for maintaining the high standard to which we have become accustomed in past years.

Protein and Amino-acid Requirements in Early Life. By L. EMMETT HOLT, JR., PAUL GYÖRGY, EDWARD L. PRATT, SELMA E. SNYDERMAN and WILLIAM M. WALLACE. (Pp. vii + 63; illustrated. $1.00.) New York University Press. 1960.

This small monograph by a distinguished team of investigators, including Professor Emmett Holt, Jr., is intended to evaluate critically the available information regarding the protein and amino-acid needs in early life, in health and disease. Much of it is based on the authors' own findings, especially on the amino-acid requirements of infants.

The clinical effects of protein deficiency, especially kwashiorkor, are discussed as well as the effects of high protein diets. To the general reader, much of the interest will lie in the section on protein requirements of infants, rather than in the individual amino-acids, admittedly of greater theoretical than practical import. The authors' conclusion is that little is gained by feeding protein diets containing more than 2·0 g. protein per kg body weight to normal full-term infants, or even to premature infants, although they are more cautious in regard to the latter.

Little mention is made of the considerable body of evidence, which has been published both in this country and the United States, in favour of a protein intake considerably greater for premature than for full-term infants. The report, however, will be useful in providing many interesting facts not easily found in the literature.

Congenital Malformations; A Ciba Foundation Symposium. Edited by G. E. W. WOLSTENHOLME. (Pp. xii + 308; 91 figures; 28 tables. 45s.) London: J. & A. Churchill. 1960.

Ciba Foundation symposia have gradually developed into authoritative discussions on subjects of current interest and importance, led by selected authorities and delivered to limited audiences. A selection in book form gives others the opportunity of having at their disposal reviews of recent work of high standard.

This volume reports the Symposium of January 1960, on 'Congenital Malformations', and contains 24 contributions, each with its own brief discussion and a final general discussion. Subjects cover a wide field and there is inevitable variation in interest and excellence. Almost, though not quite all, contributions are of absorbing interest to the general paediatrician, though the subjects tend to be treated esoterically and the reader needs to be already reasonably well up in the subject to follow the main speaker, let alone the discussion. The value in print of the discussions at the end of each chapter is debatable. Many of these make almost no additional contribution, but occasionally, as in that which follows the subject of environmental teratogenesis, the audience participate freely.

The binding, print and photo-reproductions are of American standards.

The Medical Annual. Issues 77 (pp. xl+620; 66 plates + 40 figures), 1959, and 78 (pp. li+572; 59 plates + 47 figures), 1960. Bristol: John Wright.

When stuck for some quickly available information on recent work the Medical Annual seems frequently to be able to assuage at least the worst of the need, and these two volumes for 1959 and 1960 are as useful as ever. The chapters on children's diseases review a selection of conditions, a kind of chef's collation particular to the author, Dr. Newns, but have sufficiently wide interest to make welcome food for other mouths. *Child Surgery* by R. E. Horton is largely concerned with neonatal abdominal surgery in 1959 and with various types of hernia in 1960, whilst *Child Psychiatry* by Dr. Kenneth Cameron deals with much the same subjects each year, particularly childhood dementia and the use of drugs with defective children. These three authors share between them less than 20 pages in each volume which seems inadequate and certainly limits their choice of subjects. However, articles of paediatric interest are widely dispersed throughout both volumes and, indeed, appear in almost every section.

The special articles, now a prominent feature of the Medical Annual, serve as valuable up-to-date summaries of their subject, and retain a high standard in particular

in the 1959 volume. Professor A. W. Wilkinson reviews blood and electrolyte balance in relation to surgery, much of which is directly related, or at least relevant to, childhood. Dr. Leatham this year also contributes a long article on cardiac auscultation which, read, digested and absorbed, will benefit the clinical acumen of all who read it.

The Tonsils and Adenoids in Childhood. By DONALD F. PROCTOR. (Pp. xi+70; 23 figures. 60s.) Oxford: Blackwell Scientific Publications; Springfield, Illinois: Charles C. Thomas. 1960.

This is an excellent monograph, but it is a curious commentary on present-day surgery that it should be necessary to hammer home its main message, which is given in one entry in the index—'Guillotine, avoidance of'. That is to say it pleads for the removal of tonsils and adenoids to be done with the care, accuracy and delicacy that is expected of those operating in the chest or abdomen. It is well established that what is rudely known as 'the choke and grab' method, by which some practitioners boast they can do up to 30 cases in the hour, has an enormous percentage of failures, when either too much or too little is hurriedly removed in a welter of blood. Estimates of the percentage of failures vary from 20 to 68 (Hyde, 1951), and this does not include the adenoids. Dr. Proctor confines himself, in discussing inefficiency, to the damage done by removing too little; one should consider also that done by removing too much e.g. the tight palate due to thrusting up the pillars into the ring of the guillotine, and the chronic ear discharge due to scarring of the Eustachian cushions.

For efficient operating there is needed not only technique, but also a knowledge of anatomy. I am personally flattered that the author has kind things to say about a paper in which I pointed out that the textbook descriptions of the blood supply were totally inaccurate. That account of the dangerous vessel, the paratonsillar vein, had gradually made its way into textbooks of formal anatomy, though not into those strange compilations that deal with 'surgical anatomy', nor into most textbooks of otorhinolaryngology. Consequently a far from inconsiderable number of children still bleed to death, with those responsible unaware of what vessel is bleeding; while the number of actual fatalities must be a small proportion of those which cause hours or days of acute anxiety.

Dr. Proctor states that he can find no previous account of a similar application of surgical principles to the tonsil before Dr. Crowe and his colleagues (1917) reported 1,000 tonsillectomies with 1·2% of postoperative haemorrhages. Had he departed enough from United States practice to carry his researches across the Atlantic he would have discovered that this method had been preached and practised at The Hospital for Sick Children, Great Ormond Street, for many years before 1909, when Mr. George Waugh (Waugh, 1909; Moore, 1928) who originated it, had operated on 1,500 cases (400 of which had been guillotined previously one or more times) with no haemorrhages. His paper records only 900 cases, but this was because, as he told me, it had been written two years before publication. The intervening time had been taken up in getting it past the obstruction of 'experts' who all used the guillotine and contended that the new method was so extremely dangerous that the profession should be shielded from hearing about it.

Waugh's technique was, I think, superior in that the entire removal was carried out by dissection, whereas that of Dr. Crowe descends to blind division by a snare for the last stages. And I suggest that to use a figure-of-eight suture for a bleeding vessel instead of a simple ligature carries a risk, as Dr. Proctor points out, of puncturing others hitherto intact.

The book discusses fairly the fundamental question of whether the removal of tonsils and adenoids does good or harm. The trouble is that the present percentage of operative failures renders quite futile the many investigations that have been done on this, since there is no doubt that a partial removal leaves the patient worse than before. As to whether the tonsils and adenoids have a function, or, like the mastoid cavity and similar structures, they are both useless and dangerous, Dr. Proctor is cautious. He well might be, since in this argument one is apt to encounter both the Darwinian reasoning that the universal law of survival of the fittest proves that 'they wouldn't be there if they didn't have a use' and the theological dogma which teaches that they are a part of perfection, since the human body is made in the image of God. The author rather hesitantly puts forward the usual explanation that it is good for the body to have a culture ground in which either acute or chronic infections can multiply, since in this way antibodies are formed. This line of argument is not usually applied to infected teeth or sinuses, nor to staphylococcal infections of the skin, nor to appendicitis; and it is worth noting that the almost invariable first lodging of diphtheria in the tonsil is not mentioned.

Also discussed, though not at great length, is the common infection of the adenoids and tonsils with tubercle. In this country I have sat through long conferences on the indications for their removal without hearing this spoken of, and have read recent papers on tubercular glands of the neck which omitted totally this obvious source of infection (Miller, 1956).

There is no mention of the rare but important condition of congenital adenoid obstruction which prevents proper sucking owing to the baby's inability to breathe through the nose. The removal of these adenoids requires a far smaller curette than is listed by any instrument makers but the results can be most satisfactory.

My criticisms are on minor points: the book as a whole shows a thoroughly sound surgical approach and great care for the avoidance as far as possible of fright to the patient; it should help to let in light on one of the darker departments of surgery.

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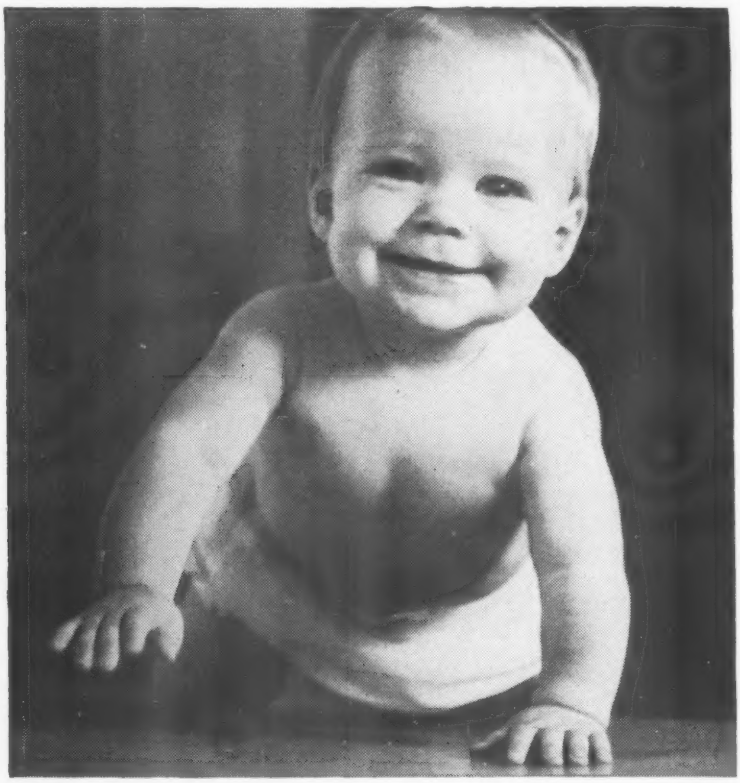

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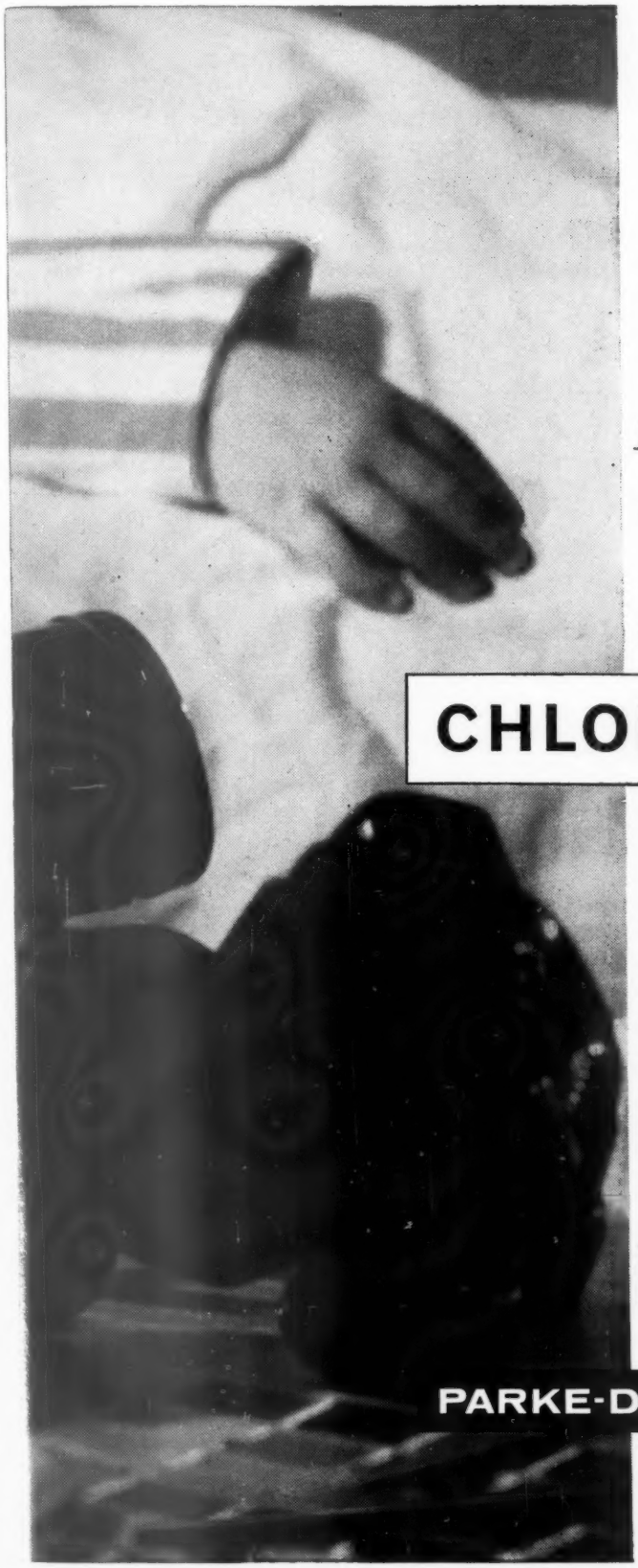

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(a) To enable a young paediatrician from any part of the Commonwealth overseas to spend six to eight weeks visiting centres in the United Kingdom, and to attend the Annual Meeting of the British Paediatric Association.

(b) To enable a young paediatrician in training in any part of the Commonwealth overseas to spend one year of post-graduate study in paediatrics, child health or in paediatric preventive medicine at approved centres in the United Kingdom. The award is not primarily intended to enable the Fellow to obtain a higher degree in medicine, but this would not be precluded.

(c) To enable a British paediatrician of registrar, senior registrar or consultative status to spend a short period at some overseas centre to study a particular problem.

Applications for these awards must be received by the Nuffield Foundation not later than 31st July, 1961.

The conditions of the Fellowships and application forms may be obtained from L. Farrer-Brown, Esq., C.B.E., J.P., Director, The Nuffield Foundation, Nuffield Lodge, Regent's Park, London, N.W.1.

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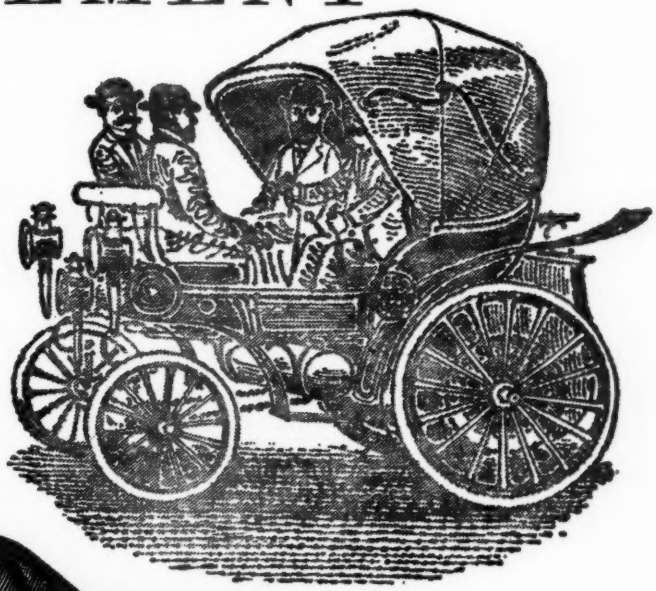

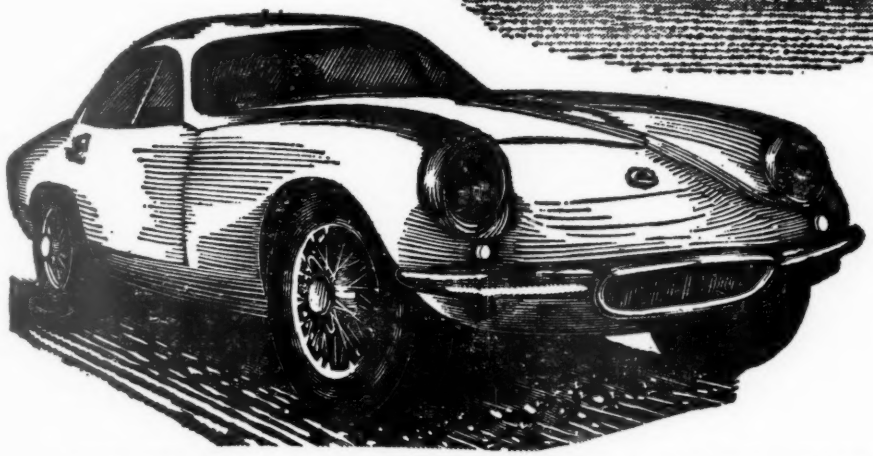

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